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(54) Title: 1,1-DISUBSTITUTED CYCLOALKYL DERIVATIVES AS FACTOR XA INHIBITORS

(57) Abstract: The present application describes 1,1-disubstituted cycloalkyl compounds and derivatives thereof, or pharmaceutically acceptable salt forms thereof, which are useful as inhibitors of factor Xa.

TITLE

1,1-Disubstituted Cycloalkyl Derivatives As Factor Xa
Inhibitors

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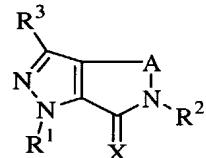
FIELD OF THE INVENTION

This invention relates generally to 1,1-disubstituted cycloalkyl compounds, which are inhibitors of trypsin-like serine protease enzymes, especially factor Xa,

10 pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

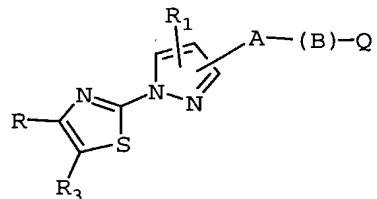
BACKGROUND OF THE INVENTION

15 U.S. Patent Nos. 3,365,459, 3,340,269, and 3,423,414 illustrate anti-inflammatory inhibitors of the following formula:



20 wherein A is 2-3 carbon atoms, X can be O, and R¹ and R³ can be substituted or unsubstituted aromatic groups. None of these patents, however, exemplify or suggest compounds of the present invention.

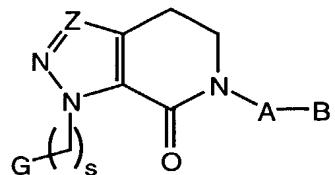
US 5,342,851 depicts thiazole platelet aggregation inhibitors including those of the following formula:



25

wherein A is a linker, B can be a linker or a ring, Q is a ring or an amino group, R, R₁, and R₃ are a variety of groups. This patent, however, does not exemplify or suggest compounds of the present invention.

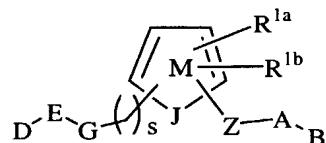
WO00/39131 describes heterobicyclic Factor Xa inhibitors of which the following is an example formula:



wherein Z is C or N, G is a mono- or bicyclic group, A is a 5 cyclic moiety and B is a basic group or a cyclic moiety.

Compounds specifically described in WO00/39131 are not considered to be part of the present invention.

WO98/28269, WO98/28282, WO99/32454, US 6,020,357, and US 6,271,237 describe Factor Xa inhibitors of the following 10 formula:



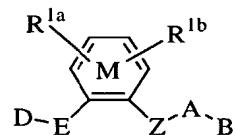
wherein ring M is a heterocycle, Z is a linker, A is a ring, B is a basic or cyclic group, D is a basic moiety, and E is a ring. Compounds specifically described in 15 WO98/28269, WO98/28282, WO99/32454, US 6,020,357, and US 6,271,237 are not considered to be part of the present invention.

WO98/57951 describes Factor Xa inhibitors of the following formula:



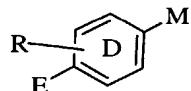
wherein ring M can be a variety of heterocycles and rings D-E represent a heterobicyclic group. Compounds 20 specifically described in WO98/57951 are not considered to be part of the present invention.

WO98/57934 and US 6,060,491 describe Factor Xa inhibitors of the following formula:



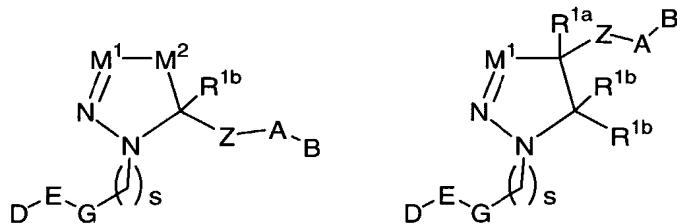
wherein ring M is a 6-membered heteroaryl, Z is a linker, A is a ring, B is a basic or cyclic group, D is a basic moiety, and E is a ring. Compounds specifically described in WO98/57934 and US 6,060,491 are not considered to be 5 part of the present invention.

WO98/57937 and US 5,998,424 describe Factor Xa inhibitors of the following formula:



wherein ring M is a variety of rings, ring D is an aromatic ring, and R and E are non-basic groups. Compounds 10 specifically described in WO98/57937 and US 5,998,424 are not considered to be part of the present invention.

WO99/50255 and US 6,191,159 describe pyrazoline and triazoline Factor Xa inhibitors of the following formulas:



Compounds specifically described in WO99/50255 and US 6,191,159 are not considered to be part of the present 15 invention.

WO00/59902 describes Factor Xa inhibitors of the 20 following formula:



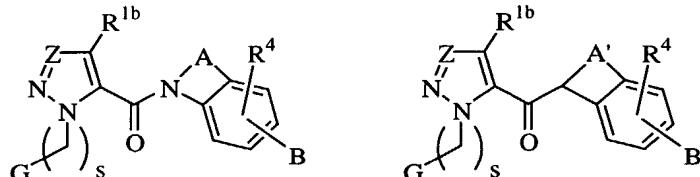
wherein ring M can be a variety of rings all of which are substituted with Z-A-B, Z is a linker, A is a ring, B is a sulfonyl-containing heterobicycle, and rings D-E represent 25 a heterobicyclic group or a 6-membered ring. Compounds specifically described in WO00/59902 are not considered to be part of the present invention.

WO01/32628 describes cyano-pyrroles, cyano-imidazoles, cyano-pyrazoles, and cyano-triazoles that are Factor Xa

inhibitors. Compounds specifically described in WO01/32628 are not considered to be part of the present invention.

WO01/05784 describes Factor Xa inhibitors of the following formulas:

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wherein Z is C or N, G is a mono- or bicyclic ring M, A is a linker, B is a basic or cyclic group. Compounds specifically described in WO01/05784 are not considered to be part of the present invention.

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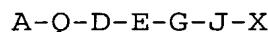
WO00/39108 describes Factor Xa inhibitors of the following formula:



15

wherein ring M can be a variety of heterocycles and rings D-E represent a heterobicyclic group. Compounds specifically described in WO00/39108 are not considered to be part of the present invention.

WO01/19798 describes factor Xa inhibitors of the following formula:



20

wherein A, D, G, and X can be phenyl or heterocycle. However, none of the presently claimed compounds are exemplified or suggested in WO01/19798.

25

Activated factor Xa, whose major practical role is the generation of thrombin by the limited proteolysis of prothrombin, holds a central position that links the intrinsic and extrinsic activation mechanisms in the final common pathway of blood coagulation. The generation of thrombin, the final serine protease in the pathway to generate a fibrin clot, from its precursor is amplified by formation of prothrombinase complex (factor Xa, factor V, Ca^{2+} and phospholipid). Since it is calculated that one molecule of factor Xa can generate 138 molecules of

thrombin (Elodi, S., Varadi, K.: Optimization of conditions for the catalytic effect of the factor IXa-factor VIII Complex: Probable role of the complex in the amplification of blood coagulation. *Thromb. Res.* **1979**, 15, 617-629), 5 inhibition of factor Xa may be more efficient than inactivation of thrombin in interrupting the blood coagulation system.

Therefore, efficacious and specific inhibitors of factor Xa are needed as potentially valuable therapeutic 10 agents for the treatment of thromboembolic disorders. It is thus desirable to discover new factor Xa inhibitors. In addition, it is also desirable to find new compounds with improved pharmacological characteristics compared with known factor Xa inhibitors. For example, it is preferred 15 to find new compounds with improved factor Xa inhibitory activity and selectivity for factor Xa versus other serine proteases (i.e., trypsin). It is also desirable and preferable to find compounds with advantageous and improved characteristics in one or more of the following categories, 20 but are not limited to: (a) pharmaceutical properties; (b) dosage requirements; (c) factors which decrease blood concentration peak-to-trough characteristics; (d) factors that increase the concentration of active drug at the receptor; (e) factors that decrease the liability for 25 clinical drug-drug interactions; (f) factors that decrease the potential for adverse side-effects; and, (g) factors that improve manufacturing costs or feasibility.

SUMMARY OF THE INVENTION

30 Accordingly, the present invention provides novel 1,1-disubstituted cycloalkyl compounds that are useful as factor Xa inhibitors or pharmaceutically acceptable salts or prodrugs thereof.

35 The present invention provides pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least

one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

The present invention provides a method for treating thromboembolic disorders comprising administering to a host 5 in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

The present invention provides a novel method of 10 treating a patient in need of thromboembolic disorder treatment, comprising: administering a compound of the present invention or a pharmaceutically acceptable salt thereof in an amount effective to treat a thromboembolic disorder.

15 The present invention provides a novel method, comprising: administering a compound of the present invention or a pharmaceutically acceptable salt thereof in an amount effective to treat a thromboembolic disorder.

The present invention provides novel compounds for use 20 in therapy.

The present invention provides the use of novel compounds for the manufacture of a medicament for the treatment of a thromboembolic disorder.

These and other objects, which will become apparent 25 during the following detailed description, have been achieved by the inventors' discovery that the presently claimed 1,1-disubstituted cycloalkyl compounds, or pharmaceutically acceptable salt or prodrug forms thereof, are effective factor Xa inhibitors.

30

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[1] In an embodiment, the present invention provides a novel compound of formula I:

35

$P_4-P-M-M_4$

I

6

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

5 M is a 3-10 membered carbocycle or a 4-10 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)_p, N, and NZ²;

ring M is substituted with 0-3 R^{1a} and 0-2 carbonyl groups, and there are 0-3 ring double bonds;

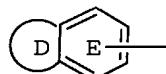
10 P is fused onto ring M and is a 5, 6, or 7 membered carbocycle or a 5, 6, or 7 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)_p, and N;

15 ring P is substituted with 0-3 R^{1a} and 0-2 carbonyl groups, and there are 0-3 ring double bonds;

20 alternatively, ring P is absent and P₄ is directly attached to ring M, provided that when ring P is absent, P₄ and M₄ are attached to the 1,2, 1,3, or 1,4 positions of ring M;

25 one of P₄ and M₄ is -Z-A-B and the other -G₁-G, provided that P₄ and M₄ are attached to different rings when ring P is present;

G is a group of formula IIa or IIb:



IIa



IIb

30 ring D, including the two atoms of Ring E to which it is attached, is a 5-6 membered ring consisting of carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p;

ring D is substituted with 0-2 R and there are 0-3 ring double bonds;

5 E is selected from phenyl, pyridyl, pyrimidyl, pyrazinyl, and pyridazinyl, and is substituted with 1-3 R;

alternatively, ring D is absent and ring E is selected from phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, 10 pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, triazolyl, thienyl, and thiazolyl, and ring E is substituted with 1-3 R;

alternatively, ring D is absent and ring E is selected from 15 phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, triazolyl, thienyl, and thiazolyl, and ring E is substituted with 1 R and with a 5-6 membered 20 heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, wherein the 5-6 membered heterocycle is substituted with 0-2 carbonyls and 1-3 R and there are 0-3 ring double bonds;

25 R is selected from H, C₁₋₄ alkyl, F, Cl, Br, I, OH, OCH₃, OCH₂CH₃, OCH(CH₃)₂, OCH₂CH₂CH₃, CN, C(=NR⁸)NR⁷R⁹, NHC(=NR⁸)NR⁷R⁹, ONHC(=NR⁸)NR⁷R⁹, NR⁸CH(=NR⁷), NH₂, NH(C₁₋₃ alkyl), N(C₁₋₃ alkyl)₂, C(=NH)NH₂, CH₂NH₂, CH₂NH(C₁₋₃ alkyl), CH₂N(C₁₋₃ alkyl)₂, CH₂CH₂NH₂, 30 CH₂CH₂NH(C₁₋₃ alkyl), CH₂CH₂N(C₁₋₃ alkyl)₂, (CR⁸R⁹)_tC(O)H, (CR⁸R⁹)_tC(O)R^{2c}, (CR⁸R⁹)_tNR⁷R⁸, (CR⁸R⁹)_tC(O)NR⁷R⁸, (CR⁸R⁹)_tNR⁷C(O)R⁷, (CR⁸R⁹)_tOR³, (CR⁸R⁹)_tS(O)_pNR⁷R⁸, (CR⁸R⁹)_tNR⁷S(O)_pR⁷, (CR⁸R⁹)_tSR³,

$(CR^8R^9)_tS(O)R^3$, $(CR^8R^9)_tS(O)_2R^3$, and OCF_3 , provided that $S(O)_pR^7$ forms other than $S(O)_2H$ or $S(O)H$;

5 alternatively, when 2 R groups are attached to adjacent atoms, they combine to form methylenedioxy or ethylenedioxy;

A is selected from:

10 C_{3-10} carbocycle substituted with 0-2 R^4 , and 5-12 membered heterocycle substituted with 0-2 R^4 and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

15 B is $Y-R^{4a}$ or $X-Y-R^{4a}$, provided that Z and B are attached to different atoms on A and A and R^{4a} or X and R^{4a} are attached to the same atom on Y;

X is selected from $-(CR^2R^{2a})_{1-4-}$, $-CR^2(CR^2R^{2b})(CH_2)_t-$,
 $-C(O)-$, $-C(=NR^{1b})-$, $-CR^2(NR^{1b}R^2)-$, $-CR^2(OR^2)-$,
 $20 -CR^2(SR^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-S(O)-$, $-S(O)_2-$,
 $-SCR^2R^{2a}-$, $-S(O)CR^2R^{2a}-$, $-S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S-$,
 $-CR^2R^{2a}S(O)-$, $-CR^2R^{2a}S(O)_2-$, $-S(O)_2NR^2-$,
 $-S(O)_2NR^2CR^2R^{2a}-$, $-CR^2R^{2a}S(O)_2NR^2-$, $-NR^2S(O)_2-$,
 $25 -CR^2R^{2a}NR^2S(O)_2-$, $-NR^2S(O)_2CR^2R^{2a}-$, $-NR^2C(O)-$,
 $-C(O)NR^2-$, $-NR^2C(O)CR^2R^{2a}-$, $-C(O)NR^2CR^2R^{2a}-$,
 $-CR^2R^{2a}NR^2C(O)-$, $-CR^2R^{2a}C(O)NR^2-$, NR^2 , $-NR^2CR^2R^{2a}-$,
 $-CR^2R^{2a}NR^2-$, O, $-OCR^2R^{2a}-$, and $-CR^2R^{2a}O-$;

30 Y is a C_{3-10} carbocycle or 3-10 membered heterocycle, wherein the carbocycle or heterocycle consists of carbon atoms and 0-4 heteroatoms selected from N, O, and $S(O)_p$, the carbocycle or heterocycle further comprises 0-4 double bonds and 0-2 carbonyl groups, and the carbocycle or heterocycle is substituted with

0-2 R⁴, provided that Y is other than a 1,3-dioxolanyl group;

alternatively, Y is CY¹Y², and Y¹ and Y² are independently
 5 C₁₋₄ alkyl substituted with 0-2 R⁴;

G₁ is absent or is selected from (CR³R^{3a})₁₋₅,

(CR³R^{3a})₀₋₂CR³=CR³ (CR³R^{3a})₀₋₂, (CR³R^{3a})₀₋₂C≡C (CR³R^{3a})₀₋₂,
 10 (CR³R^{3a})_uC(O) (CR³R^{3a})_w, (CR³R^{3a})_uC(O)O (CR³R^{3a})_w,
 (CR³R^{3a})_uOC(O) (CR³R^{3a})_w, (CR³R^{3a})_uO (CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}(CR³R^{3a})_w, (CR³R^{3a})_uC(O)NR^{3b}(CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}C(O) (CR³R^{3a})_w, (CR³R^{3a})_uOC(O)NR^{3b}(CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}C(O)O (CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}C(O)NR^{3b}(CR³R^{3a})_w,
 15 (CR³R^{3a})_uNR^{3b}C(S)NR^{3b}(CR³R^{3a})_w, (CR³R^{3a})_uS(CR³R^{3a})_w,
 (CR³R^{3a})_uS(O) (CR³R^{3a})_w, (CR³R^{3a})_uS(O)₂(CR³R^{3a})_w,
 (CR³R^{3a})_uS(O)NR^{3b}(CR³R^{3a})_w, (CR³R^{3a})_uNR^{3b}S(O)₂(CR³R^{3a})_w,
 (CR³R^{3a})_uS(O)₂NR^{3b}(CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}S(O)₂NR^{3b}(CR³R^{3a})_w, (CR³R^{3a})_uNR^{3e}(CR³R^{3a})_w,
 20 (CR³R^{3a})_uC(O) (CR³R^{3a})_uC(O) (CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}(CR³R^{3a})_uC(O)NR^{3b}(CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}C(O) (CR³R^{3a})_uC(O) (CR³R^{3a})_w,
 (CR³R^{3a})_uC(O) (CR³R^{3a})_uC(O)NR^{3b}(CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}C(O) (CR³R^{3a})_uC(O)NR^{3b}(CR³R^{3a})_w,
 25 (CR³R^{3a})_uNR^{3b}bC(S) (CR³R^{3a})_uC(O)NR^{3b}(CR³R^{3a})_w,
 (CR³R^{3a})_uNR^{3b}C(O) (CR³R^{3a})_uC(S)NR^{3b}(CR³R^{3a})_w,
 (CR³R^{3a})_uS(O)NR^{3b}C(O) (CR³R^{3a})_w,
 (CR³R^{3a})_uC(O)NR^{3b}S(O)₂(CR³R^{3a})_w, and
 (CR³R^{3a})_uS(O)₂NR^{3b}C(O)NR^{3b}(CR³R^{3a})_w, wherein u + w total
 30 0, 1, 2, 3, or 4, provided that G₁ does not form a N-S, NCH₂N, NCH₂O, or NCH₂S bond with either group to which it is attached;

Z is selected from a bond, $-(CR^3R^{3e})_{1-4}-$,

$(CR^3R^{3e})_qO(CR^3R^{3e})_{q1}$, $(CR^3R^{3e})_qNR^{3b}(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qC(O)(CR^3R^{3e})_{q1}$, $(CR^3R^{3e})_qC(O)O(CR^3R^{3e})_{q1}$,

5 $(CR^3R^{3e})_qOC(O)(CR^3R^{3e})_{q1}$, $(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qNR^{3b}C(O)(CR^3R^{3e})_{q1}$, $(CR^3R^{3e})_qOC(O)O(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qOC(O)NR^{3b}(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qNR^{3b}C(O)O(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qNR^{3b}C(O)NR^{3b}(CR^3R^{3e})_{q1}$,

10 $(CR^3R^{3e})_qC(O)(CR^3R^{3e})_qC(O)(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qNR^{3b}(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qNR^{3b}C(O)(CR^3R^{3e})_qC(O)(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qC(O)(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qNR^{3b}C(O)(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$,

15 $(CR^3R^{3e})_qS(CR^3R^{3e})_{q1}$, $(CR^3R^{3e})_qS(O)(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qS(O)_2(CR^3R^{3e})_{q1}$, $(CR^3R^{3e})_qSO_2NR^{3b}(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qNR^{3b}SO_2(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qS(O)NR^{3b}C(O)(CR^3R^{3e})_{q1}$,

$(CR^3R^{3e})_qC(O)NR^{3b}S(O)_2(CR^3R^{3e})_{q1}$, and

20 $(CR^3R^{3e})_qNR^{3b}SO_2NR^{3b}(CR^3R^{3e})_{q1}$, wherein q + q1 total 0,

1, 2, 3, or 4, provided that Z does not form a N-S,

NCH₂N, NCH₂O, or NCH₂S bond with either group to which it is attached;

25 provided that:

(a) when ring P is absent and ring M is a pyridyl ring, then Z is other than C(O)NHCH₂; and,

(b) when ring P is absent and ring M is a piperazinyl ring, then either Z is other than alkylene or A is other

30 than phenyl;

Z^2 is selected from H, S(O)₂NHR^{3b}, C(O)R^{3b}, C(O)NHR^{3b}, C(O)OR^{3f}, S(O)R^{3f}, S(O)₂R^{3f}, C₁₋₆ alkyl substituted with

0-2 R^{1a} , C_{2-6} alkenyl substituted with 0-2 R^{1a} , C_{2-6} alkynyl substituted with 0-2 R^{1a} , $-(C_{0-4}$ alkyl $)-C_{3-10}$ carbocycle substituted with 0-3 R^{1a} , and $-(C_{0-4}$ alkyl $)-5-10$ membered heterocycle substituted with 0-3 R^{1a} and 5 consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

R^{1a} , at each occurrence, is selected from H, $-(CR^3R^{3a})_r-R^{1b}$, $-(CR^3R^{3a})_r-CR^3R^{1b}R^{1b}$, $-(CR^3R^{3a})_r-O-(CR^3R^{3a})_r-R^{1b}$, 10 $-(CR^3R^{3a})_r-NR^2-(CR^3R^{3a})_r-R^{1b}$, $-(CR^3R^{3a})_r-S(O)_p-(CR^3R^{3a})_r-R^{1b}$, $-(CR^3R^{3a})_r-CO_2-(CR^3R^{3a})_r-R^{1b}$, $-(CR^3R^{3a})_r-C(O)NR^2-(CR^3R^{3a})_r-R^{1b}$, $-(CR^3R^{3a})_r-C(O)-(CR^3R^{3a})_r-R^{1b}$, $-C_{2-6}$ alkenylene- R^{1b} , 15 $-C_{2-6}$ alkynylene- R^{1b} , and $-(CR^3R^{3a})_r-C(=NR^{1b})NR^3R^{1b}$, provided that R^{1a} forms other than an N-halo, N-S, O-O, or N-CN bond;

alternatively, when two R^{1a} groups are attached to adjacent 20 atoms or to the same carbon atom, together with the atoms to which they are attached, they form a 5-7 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$, this ring being substituted with 0-2 R^{4b} 25 and comprising: 0-3 double bonds;

R^{1b} is selected from H, C_{1-3} alkyl, F, Cl, Br, I, -CN, $-NO_2$, $-CHO$, $(CF_2)_rCF_3$, $(CR^3R^{3a})_rOR^2$, NR^2R^{2a} , $C(O)R^{2b}$, CO_2R^{2b} , $OC(O)R^2$, $CH(CH_2OR^2)_2$, $(CF_2)_rCO_2R^{2a}$, $S(O)_pR^{2b}$, 30 $NR^2(CH_2)_rOR^2$, $C(=NR^{2c})NR^2R^{2a}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $NR^2C(O)_2R^{2a}$, $OC(O)NR^2R^{2a}$, $C(O)NR^2R^{2a}$, $C(O)NR^2(CH_2)_rOR^2$, $SO_2NR^2R^{2a}$, $NR^2SO_2R^2$, $C(O)NR^2SO_2R^2$, C_{3-6} carbocycle substituted with 0-2 R^{4b} , and 5-10 membered heterocycle

substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{1b} forms other than an O-O, N-halo, N-S, or N-CN bond and
5 provided that S(O)_pR² forms other than S(O)₂H or S(O)H;

R², at each occurrence, is selected from H, CF₃, C₁₋₆ alkyl, benzyl, -(CH₂)_r-C₃₋₁₀ carbocycle substituted with 0-2 R^{4b}, and -(CH₂)_r-5-10 membered heterocycle substituted
10 with 0-2 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2a}, at each occurrence, is selected from H, CF₃, C₁₋₆ alkyl, benzyl, -(CH₂)_r-C₃₋₁₀ carbocycle substituted with 0-2 R^{4b}, and -(CH₂)_r-5-10 membered heterocycle substituted with 0-2 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

20 alternatively, R² and R^{2a}, together with the nitrogen atom to which they are attached, combine to form a 3-6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2b}, at each occurrence, is selected from CF₃, C₁₋₄ alkoxy substituted with 0-2 R^{4b}, C₁₋₆ alkyl substituted with 0-3 R^{4b}, -(CH₂)_r-C₃₋₁₀ carbocycle substituted with 0-2 R^{4b}, and -(CH₂)_r-5-10 membered heterocycle substituted with 0-2 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

5 R^{2c} , at each occurrence, is selected from CF_3 , OH , C_{1-4} alkoxy, C_{1-6} alkyl, $-(CH_2)_r-C_{3-10}$ carbocycle substituted with 0-2 R^{4b} , and $-(CH_2)_r-5-10$ membered heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N , O , and $S(O)_p$;

10 R^{2d} , at each occurrence, is selected from H , R^{4c} , C_{1-6} alkyl substituted with 0-2 R^{4c} , $-(CR^3R^{3a})_r-C_{3-10}$ carbocycle substituted with 0-2 R^{4c} , and $-(CR^3R^{3a})_r-5-10$ membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N , O , and $S(O)_p$, provided that R^{2d} 15 forms other than a N -halo, $N-C$ -halo, $S(O)_p$ -halo, O -halo, $N-S$, $S-N$, $S(O)_p-S(O)_p$, $S-O$, $O-N$, $O-S$, or $O-O$ moiety;

20 alternatively, when two R^{2d} 's are attached to the same nitrogen atom, then R^{2d} and R^{2d} , together with the nitrogen atom to which they are attached, combine to form a 5-10 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and consisting of: 0-1 additional heteroatoms selected 25 from the group consisting of N , O , and $S(O)_p$;

30 R^{2e} , at each occurrence, is selected from H , R^{4c} , C_{1-6} alkyl substituted with 0-2 R^{4c} , $-(CR^3R^{3a})_r-C_{3-10}$ carbocycle substituted with 0-2 R^{4c} , and $-(CR^3R^{3a})_r-5-10$ membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N , O , and $S(O)_p$, provided that R^{2e} forms other than a $C(O)$ -halo or $C(O)-S(O)_p$ moiety;

R^3 , at each occurrence, is selected from H, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, benzyl, and phenyl;

5 R^{3a} , at each occurrence, is selected from H, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, benzyl, and phenyl;

10 alternatively, R^3 and R^{3a} , together with the nitrogen atom
to which they are attached, combine to form a 5 or 6
membered saturated, partially unsaturated, or
unsaturated ring consisting of: carbon atoms, the
nitrogen atom to which R^3 and R^{3a} are attached, and 0-1
additional heteroatoms selected from the group
15 consisting of N, O, and $S(O)_p$;

20 R^{3b} , at each occurrence, is selected from H, C₁₋₆ alkyl
substituted with 0-2 R^{1a} , C₂₋₆ alkenyl substituted with
0-2 R^{1a} , C₂₋₆ alkynyl substituted with 0-2 R^{1a} , -(C₀₋₄
alkyl)-5-10 membered carbocycle substituted with 0-3
 R^{1a} , and -(C₀₋₄ alkyl)- 5-10 membered heterocycle
substituted with 0-3 R^{1a} and consisting of: carbon
atoms and 1-4 heteroatoms selected from the group
consisting of N, O, and $S(O)_p$;

25 R^{3c} , at each occurrence, is selected from CH_3 , CH_2CH_3 ,
 $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$,
 $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, benzyl, and phenyl;

30 R^{3d} , at each occurrence, is selected from H, CH_3 , CH_2CH_3 ,
 $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$,
 $CH(CH_3)CH_2CH_3$, C₁₋₄ alkyl-phenyl, and $C(=O)R^{3c}$;

R^{3e} , at each occurrence, is selected from H, $S(O)_2NHR^3$, $C(O)R^3$, $C(O)NHR^3$, $C(O)OR^{3f}$, $S(O)R^{3f}$, $S(O)_2R^{3f}$, C_{1-6} alkyl substituted with 0-2 R^{1a} , C_{2-6} alkenyl substituted with 0-2 R^{1a} , C_{2-6} alkynyl substituted with 0-2 R^{1a} , $-(C_{0-4}$ alkyl)-5-10 membered carbocycle substituted with 0-3 R^{1a} , and $-(C_{0-4}$ alkyl)-5-10 membered heterocycle substituted with 0-3 R^{1a} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

10

R^{3f} , at each occurrence, is selected from: C_{1-6} alkyl substituted with 0-2 R^{1a} , C_{2-6} alkenyl substituted with 0-2 R^{1a} , C_{2-6} alkynyl substituted with 0-2 R^{1a} , $-(C_{0-4}$ alkyl)-5-10 membered carbocycle substituted with 0-3 R^{1a} , and $-(C_{0-4}$ alkyl)-5-10 membered heterocycle substituted with 0-3 R^{1a} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

20 R^{3g} , at each occurrence, is selected from H, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, $-(CH_2)_r-3-6$ memberedcarbocycle, and $-(CH_2)_r-5-6$ membered heterocycle

consisting of: carbon atoms and 1-4 heteroatoms

25 selected from the group consisting of N, O, and $S(O)_p$;

alternatively, when R^3 and R^{3g} are attached to the same carbon atom, they combine with the attached carbon atom to form a cyclopropyl group;

30

R^4 , at each occurrence, is selected from H, =O, $(CR^3R^{3a})_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, $(CR^3R^{3a})_rCN$, $(CR^3R^{3a})_rNO_2$, $(CR^3R^{3a})_rNR^2R^{2a}$, $(CR^3R^{3a})_rC(O)R^{2c}$,

$(CR^3R^{3a})_rNR^2C(O)R^{2b}$, $(CR^3R^{3a})_rC(O)NR^2R^{2a}$,
 $(CR^3R^{3a})_rNR^2C(O)NR^2R^{2a}$, $(CR^3R^{3a})_rC(=NR^2)NR^2R^{2a}$,
 $(CR^3R^{3a})_rC(=NS(O)_2R^{5a})NR^2R^{2a}$, $(CR^3R^{3a})_rNR^2C(=NR^2)NR^2R^{2a}$,
 $(CR^3R^{3a})_rC(O)NR^2C(=NR^2)NR^2R^{2a}$, $(CR^3R^{3a})_rSO_2NR^2R^{2a}$,
5 $(CR^3R^{3a})_rNR^2SO_2NR^2R^{2a}$, $(CR^3R^{3a})_rNR^2SO_2-C_{1-4}$ alkyl,
 $(CR^3R^{3a})_rNR^2SO_2R^{5a}$, $(CR^3R^{3a})_rS(O)_pR^{5a}$, $(CR^3R^{3a})_r(CF_2)_rCF_3$,
 $N(CH_2)_rR^{1b}$, $O(CH_2)_rR^{1b}$, $S(CH_2)_rR^{1b}$, $(CR^3R^{3a})_r-5-6$
 membered carbocycle substituted with 0-1 R^5 , and a
 $(CR^3R^{3a})_r-5-6$ membered heterocycle substituted with 0-1
10 R^5 and consisting of: carbon atoms and 1-4
 heteroatoms selected from the group consisting of N,
 O , and $S(O)_p$;

R^{4a} is selected from C_{1-6} alkyl substituted with 0-2 R^{4c} ,
15 C_{2-6} alkenyl substituted with 0-2 R^{4c} , C_{2-6} alkynyl
 substituted with 0-2 R^{4c} , $-(CR^3R^{3g})_r-C_{5-10}$ membered
 carbocycle substituted with 0-3 R^{4c} , $-(CR^3R^{3g})_r-5-10$
 membered heterocycle substituted with 0-3 R^{4c} and
 consisting of: carbon atoms and 1-4 heteroatoms
20 selected from the group consisting of N, O, and $S(O)_p$,
 $(CR^3R^{3g})_rCN$, $(CR^3R^{3g})_rC(=NR^{2d})NR^{2d}R^{2d}$,
 $(CR^3R^{3g})_rNR^{2d}C(=NR^{2d})NR^{2d}R^{2d}$, $(CR^3R^{3g})_rNR^{2d}C(R^{2e})(=NR^{2d})$,
 $(CR^3R^{3g})_rNR^{2d}R^{2d}$, $(CR^3R^{3g})_rN(\rightarrow O)R^{2d}R^{2d}$, $(CR^3R^{3g})_rOR^{2d}$,
 $(CR^3R^{3g})_r-NR^{2d}C(O)R^{2e}$, $(CR^3R^{3g})_r-C(O)R^{2e}$,
25 $(CR^3R^{3g})_r-OC(O)R^{2e}$, $(CR^3R^{3g})_r-C(O)NR^{2d}R^{2d}$,
 $(CR^3R^{3g})_r-C(O)OR^{2d}$, $(CR^3R^{3g})_r-NR^{2d}C(O)NR^{2d}R^{2d}$,
 $(CR^3R^{3g})_r-OC(O)NR^{2d}R^{2d}$, $(CR^3R^{3g})_r-NR^{2d}C(O)OR^{2d}$,
 $(CR^3R^{3g})_r-SO_2NR^{2d}R^{2d}$, $(CR^3R^{3g})_r-NR^{2d}SO_2NR^{2d}R^{2d}$,
 $(CR^3R^{3g})_r-C(O)NR^{2d}SO_2R^{2d}$, $(CR^3R^{3g})_r-NR^{2d}SO_2R^{2d}$, and
30 $(CR^3R^{3g})_r-S(O)_pR^{2d}$, provided that $S(O)_pR^{2d}$ forms other
 than $S(O)_2H$ or $S(O)H$ and further provided that R^{4a} is
 other than a hydroxamic acid;

R^{4b} , at each occurrence, is selected from H, =O, $(CH_2)_rOR^3$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, 5 $(CH_2)_rC(O)OR^{3c}$, $(CH_2)_rNR^3C(O)R^{3a}$, $(CH_2)_r-C(O)NR^3R^{3a}$, $(CH_2)_rNR^3C(O)NR^3R^{3a}$, $(CH_2)_r-C(=NR^3)NR^3R^{3a}$, $(CH_2)_rNR^3C(=NR^3)NR^3R^{3a}$, $(CH_2)_rSO_2NR^3R^{3a}$, $(CH_2)_rNR^3SO_2NR^3R^{3a}$, $(CH_2)_rNR^3SO_2-C_{1-4}$ alkyl, $(CH_2)_rNR^3SO_2CF_3$, $(CH_2)_rNR^3SO_2$ -phenyl, $(CH_2)_rS(O)_pCF_3$, 10 $(CH_2)_rS(O)_p-C_{1-4}$ alkyl, $(CH_2)_rS(O)_p$ -phenyl, and $(CH_2)_r(CF_2)_rCF_3$;

R^{4c} , at each occurrence, is selected from =O, $(CR^3R^{3a})_rOR^2$, $(CR^3R^{3a})_rF$, $(CR^3R^{3a})_rBr$, $(CR^3R^{3a})_rCl$, $(CR^3R^{3a})_rCF_3$, C_{1-4} 15 alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $(CR^3R^{3a})_rCN$, $(CR^3R^{3a})_rNO_2$, $(CR^3R^{3a})_rNR^2R^{2a}$, $(CR^3R^{3a})_rN(\rightarrow O)R^2R^{2a}$, $(CR^3R^{3a})_rC(O)R^{2c}$, $(CR^3R^{3a})_rNR^2C(O)R^{2b}$, $(CR^3R^{3a})_rC(O)NR^2R^{2a}$, $(CR^3R^{3a})_rN=CHOR^3$, $(CR^3R^{3a})_rC(O)NR^2(CH_2)_2NR^2R^{2a}$, $(CR^3R^{3a})_rNR^2C(O)NR^2R^{2a}$, 20 $(CR^3R^{3a})_rC(=NR^2)NR^2R^{2a}$, $(CR^3R^{3a})_rNR^2C(=NR^2)NR^2R^{2a}$, $(CR^3R^{3a})_rSO_2NR^2R^{2a}$, $(CR^3R^{3a})_rNR^2SO_2NR^2R^{2a}$, $(CR^3R^{3a})_rC(O)NR^2SO_2-C_{1-4}$ alkyl, $(CR^3R^{3a})_rNR^2SO_2R^{5a}$, $(CR^3R^{3a})_rS(O)_pR^{5a}$, $(CF_2)_rCF_3$, $(CR^3R^{3a})_rC_{3-10}$ carbocycle 25 substituted with 0-2 R^{4b} , and $(CR^3R^{3a})_r4-10$ membered heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

R^5 , at each occurrence, is selected from H, C_{1-6} alkyl, =O, 30 $(CH_2)_rOR^3$, F, Cl, Br, I, -CN, NO_2 , $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $(CH_2)_rNR^3C(O)R^{3a}$, $(CH_2)_rC(O)NR^3R^{3a}$, $(CH_2)_rNR^3C(O)NR^3R^{3a}$, $(CH_2)_rCH(=NOR^{3d})$,

$(CH_2)_rC(=NR^3)NR^3R^{3a}$, $(CH_2)_rNR^3C(=NR^3)NR^3R^{3a}$,
 $(CH_2)_rSO_2NR^3R^{3a}$, $(CH_2)_rNR^3SO_2NR^3R^{3a}$, $(CH_2)_rNR^3SO_2-C_{1-4}$
 alkyl, $(CH_2)_rNR^3SO_2CF_3$, $(CH_2)_rNR^3SO_2$ -phenyl,
 $(CH_2)_rS(O)_pCF_3$, $(CH_2)_rS(O)_p-C_{1-4}$ alkyl, $(CH_2)_rS(O)_p$ -
 5 phenyl, $(CF_2)_rCF_3$, phenyl substituted with 0-2 R^6 ,
 naphthyl substituted with 0-2 R^6 , and benzyl
 substituted with 0-2 R^6 ;

 R^{5a} , at each occurrence, is selected from C_{1-6} alkyl,
 10 $(CH_2)_rOR^3$, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$,
 $(CH_2)_rNR^3C(O)R^{3a}$, $(CH_2)_rC(O)NR^3R^{3a}$, $(CF_2)_rCF_3$, phenyl
 substituted with 0-2 R^6 , naphthyl substituted with 0-2
 R^6 , and benzyl substituted with 0-2 R^6 , provided that
 R^{5a} does not form a S-N or $S(O)_p-C(O)$ bond;

 15 R^6 , at each occurrence, is selected from H, OH, $(CH_2)_rOR^2$,
 halo, C_{1-4} alkyl, -CN, NO_2 , $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2b}$,
 $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $C(=NH)NH_2$, $NHC(=NH)NH_2$,
 $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, and $NR^2SO_2C_{1-4}$ alkyl;

 20 R^7 , at each occurrence, is selected from H, OH, C_{1-6} alkyl,
 C_{1-6} alkyl- $C(O)-$, C_{1-6} alkyl- $O-$, $(CH_2)_n$ -phenyl, C_{1-4}
 alkyl- $OC(O)-$, C_{6-10} aryl- $O-$, C_{6-10} aryl- $OC(O)-$, C_{6-10}
 aryl- $CH_2-C(O)-$, C_{1-4} alkyl- $C(O)O-C_{1-4}$ alkyl- $OC(O)-$,
 25 C_{6-10} aryl- $C(O)O-C_{1-4}$ alkyl- $OC(O)-$,
 C_{1-6} alkyl- $NH_2-C(O)-$, phenyl- $NH_2-C(O)-$, and phenyl C_{1-4}
 alkyl- $C(O)-$;

 30 R^8 , at each occurrence, is selected from H, C_{1-6} alkyl, and
 $(CH_2)_n$ -phenyl;

 alternatively, R^7 and R^8 , when attached to the same
 nitrogen, combine to form a 5-10 membered heterocyclic

ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and S(O)_p;

5 R⁹, at each occurrence, is selected from H, C₁₋₆ alkyl, and (CH₂)_n-phenyl;

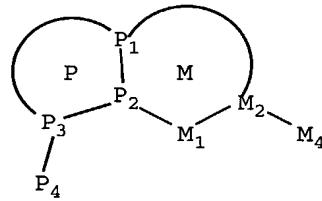
n, at each occurrence, is selected from 0, 1, 2, and 3;

10 p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, 3, 4, 5, and 6; and,

15 t, at each occurrence, is selected from 0, 1, 2, and 3.

[2] In a preferred embodiment, the present invention provides a novel compound of Formula II:



20

II

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

25 ring M, including P₁, P₂, M₁, and M₂, is a 5, 6, or 7 membered carbocycle or a 5, 6, or 7 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)_p, N, and NZ²;

30 ring M is substituted with 0-2 R^{1a} and 0-2 carbonyl groups, and there are 0-3 ring double bonds;

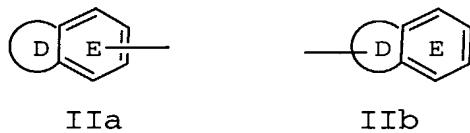
ring P, including P₁, P₂, and P₃, is a 5 or 6 membered aromatic heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)_p, and N;

5 alternatively, ring P, including P₁, P₂, and P₃, is a 5 or 6
6 membered dihydro-aromatic heterocycle, consisting of:
carbon atoms and 1-3 heteroatoms selected from O,
S(O)_p, and N;

10 ring P is substituted with 0-2 R^{1a};

one of P_4 and M_4 is $-Z-A-B$ and the other $-G_1-G$;

G is a group of formula IIa or IIb:



ring D, including the two atoms of Ring E to which it is attached, is a 5-6 membered ring consisting of carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)_p;

ring D is substituted with 0-2 R and there are 0-3 ring double bonds;

25 E is selected from phenyl, pyridyl, pyrimidyl, pyrazinyl, and pyridazinyl, and is substituted with 1-3 R;

alternatively, ring D is absent, and ring E is selected from phenyl, pyridyl, pyrimidyl, and thiienyl, and ring E is substituted with 1-3 R;

alternatively, ring D is absent, ring E is selected from phenyl, pyridyl, and thiienyl, and ring E is substituted with 1 R and substituted with a 5-6

membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, wherein the 5-6 membered heterocycle is substituted with 0-2 carbonyls and 1-3 R and there
5 are 0-3 ring double bonds;

R is selected from H, C₁₋₄ alkyl, F, Cl, OH, OCH₃, OCH₂CH₃, OCH(CH₃)₂, CN, C(=NH)NH₂, C(=NH)NHOH, C(=NH)NHOCH₃, NH₂, NH(C₁₋₃ alkyl), N(C₁₋₃ alkyl)₂, C(=NH)NH₂, CH₂NH₂,
10 CH₂NH(C₁₋₃ alkyl), CH₂N(C₁₋₃ alkyl)₂, (CR⁸R⁹)_tNR⁷R⁸, C(O)NR⁷R⁸, CH₂C(O)NR⁷R⁸, S(O)_pNR⁷R⁸, CH₂S(O)_pNR⁷R⁸, SO₂R³, and OCF₃;

alternatively, when 2 R groups are attached to adjacent
15 atoms, they combine to form methylenedioxy or ethylenedioxy;

A is selected from:

C₅₋₁₀ carbocycle substituted with 0-2 R⁴, and
20 5-10 membered heterocycle substituted with 0-2 R⁴ and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

X is selected from -(CR²R^{2a})₁₋₄-, -C(O)-, -C(O)CR²R^{2a}-,
25 -CR²R^{2a}C(O), -S(O)₂-, -S(O)₂CR²R^{2a}-, -CR²R^{2a}S(O)₂-, -NR²S(O)₂-, -S(O)₂NR²-, -NR²C(O)-, -C(O)NR²-, NR², -NR²CR²R^{2a}-, -CR²R^{2a}NR²-, O, -OCR²R^{2a}-, and -CR²R^{2a}O-;

Y is a C₃₋₇ monocyclic carbocycle or 3-7 membered monocyclic heterocycle, wherein the carbocycle or heterocycle consists of: carbon atoms and 0-2 heteroatoms selected from N, O, and S(O)_p, the carbocycle or heterocycle further comprises 0-2 double bonds and 0-2

carbonyl groups, and the carbocycle or heterocycle is substituted with 0-2 R⁴;

alternatively, Y is CY¹Y², and Y¹ and Y² are independently
5 C₁₋₃ alkyl substituted with 0-1 R⁴;

Z is selected from a bond, CH₂, CH₂CH₂, CH₂O, OCH₂, C(O),
NH, CH₂NH, NHCH₂, CH₂C(O), C(O)CH₂, C(O)NH, NHC(O),
NHC(O)CH₂C(O)NH, S(O)₂, CH₂S(O)₂, S(O)₂(CH₂), SO₂NH,
10 and NHSO₂, provided that Z does not form a N-S, NCH₂N,
NCH₂O, or NCH₂S bond with either group to which it is
attached;

Z² is selected from H, C₁₋₄ alkyl, phenyl, benzyl, C(O)R^{3b},
15 S(O)R^{3f}, and S(O)₂R^{3f};

R^{1a}, at each occurrence, is selected from H, -(CH₂)_r-R^{1b},
-(CH(CH₃))_r-R^{1b}, -(C(CH₃)₂)_r-R^{1b}, -O-(CR³R^{3a})_r-R^{1b},
-NR²-(CR³R^{3a})_r-R^{1b}, and -S-(CR³R^{3a})_r-R^{1b}, provided that
20 R^{1a} forms other than an N-halo, N-S, O-O, or N-CN bond;

alternatively, when two R^{1a} groups are attached to adjacent
atoms or to the same carbon atom, together with the
atoms to which they are attached, they form a 5-7
25 membered ring consisting of: carbon atoms and 0-2
heteroatoms selected from the group consisting of N,
O, and S(O)_p, this ring being substituted with 0-2 R^{4b}
and comprising: 0-3 double ring bonds;

30 R^{1b} is selected from H, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, F,
Cl, Br, I, -CN, -CHO, CF₃, OR², NR²R^{2a}, C(O)R^{2b}, CO₂R^{2b},
OC(O)R², CO₂R^{2a}, S(O)_pR^{2b}, NR²(CH₂)_rOR², NR²C(O)R^{2b},
NR²C(O)NHR², NR²C(O)₂R^{2a}, OC(O)NR²R^{2a}, C(O)NR²R^{2a},

C(O)NR²(CH₂)_rOR², SO₂NR²R^{2a}, NR²SO₂R², C₅₋₆ carbocycle substituted with 0-2 R^{4b}, and 5-6 membered heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group
5 consisting of N, O, and S(O)_p, provided that R^{1b} forms other than an O-O, N-halo, N-S, or N-CN bond and provided that S(O)_pR² forms other than S(O)₂H or S(O)H;

R², at each occurrence, is selected from H, CF₃, CH₃,
10 CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂CH₂CH₂CH₃, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, C(CH₃)₃, benzyl, C₅₋₆ carbocycle substituted with 0-2 R^{4b}, a C₅₋₆ carbocycle-CH₂- substituted with 0-2 R^{4b}, and 5-6 membered heterocycle substituted with 0-2 R^{4b} and consisting of: carbon
15 atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2a}, at each occurrence, is selected from H, CF₃, CH₃,
CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂CH₂CH₂CH₃, CH₂CH(CH₃)₂,
20 CH(CH₃)CH₂CH₃, C(CH₃)₃, benzyl, C₅₋₆ carbocycle substituted with 0-2 R^{4b}, and 5-6 membered heterocycle substituted with 0-2 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

25 alternatively, R² and R^{2a}, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2b}, at each occurrence, is selected from CF₃, C₁₋₄ alkoxy, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂CH₂CH₂CH₃,

CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, C(CH₃)₃, benzyl, C₅₋₆ carbocycle substituted with 0-2 R^{4b}, and 5-6 membered heterocycle substituted with 0-2 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

5 R^{2c}, at each occurrence, is selected from CF₃, OH, C₁₋₄ alkoxy, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂CH₂CH₂CH₃, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, C(CH₃)₃, benzyl, C₅₋₆ carbocycle substituted with 0-2 R^{4b}, and 5-6 membered heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

10 15 R^{2d}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, -(CR³R^{3a})_r-C₃₋₆ carbocycle substituted with 0-2 R^{4c}, and -(CR³R^{3a})_r-5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2d} forms other than a N-halo, N-C-halo, S(O)_p-halo, O-halo, N-S, S-N, S(O)_p-S(O)_p, S-O, O-N, O-S, or O-O moiety;

20 25 alternatively, when two R^{2d}'s are attached to the same nitrogen atom, then R^{2d} and R^{2d}, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)_p;

30 R^{2e}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, -(CR³R^{3a})_r-C₃₋₆ carbocycle

substituted with 0-2 R^{4c}, and -(CR³R^{3a})_r-5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2e} forms other than a C(O)-halo or C(O)-S(O)_p moiety;

5 R³, at each occurrence, is selected from H, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, and phenyl;

10 R^{3a}, at each occurrence, is selected from H, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, and phenyl;

15 alternatively, R³ and R^{3a}, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially unsaturated, or unsaturated ring consisting of: carbon atoms and the nitrogen atom to which R³ and R^{3a} are attached;

20 R^{3c}, at each occurrence, is selected from CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, and phenyl;

25 R^{3d}, at each occurrence, is selected from H, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂-phenyl, CH₂CH₂-phenyl, and C(=O)R^{3c};

30 R^{3g}, at each occurrence, is selected from H, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, cyclopropyl, cyclopropyl-methyl, benzyl, and phenyl;

35 alternatively, when R³ and R^{3g} are attached to the same carbon atom, they combine with the attached carbon atom to form a cyclopropyl group;

R^4 , at each occurrence, is selected from H, =O, OR², CH₂OR², (CH₂)₂OR², F, Cl, Br, I, C₁₋₄ alkyl, -CN, NO₂, NR²R^{2a}, CH₂NR²R^{2a}, (CH₂)₂NR²R^{2a}, C(O)R^{2c}, NR²C(O)R^{2b}, C(O)NR²R^{2a}, SO₂NR²R^{2a}, S(O)_pR^{5a}, CF₃, CF₂CF₃, 5-6 membered

5 carbocycle substituted with 0-1 R⁵, and a 5-6 membered heterocycle substituted with 0-1 R⁵ and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

10 R^{4b}, at each occurrence, is selected from H, =O, OR³, CH₂OR³, F, Cl, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂CH₂CH₂CH₃, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, C(CH₃)₃, -CN, NO₂, NR³R^{3a}, CH₂NR³R^{3a}, C(O)R³, CH₂-C(O)R³, C(O)OR^{3c}, CH₂C(O)OR^{3c}, NR³C(O)R^{3a}, CH₂NR³C(O)R^{3a}, C(O)NR³R^{3a}, 15 CH₂C(O)NR³R^{3a}, NR³C(O)NR³R^{3a}, CH₂NR³C(O)NR³R^{3a}, C(=NR³)NR³R^{3a}, CH₂C(=NR³)NR³R^{3a}, NR³C(=NR³)NR³R^{3a}, CH₂NR³C(=NR³)NR³R^{3a}, SO₂NR³R^{3a}, CH₂SO₂NR³R^{3a}, NR³SO₂NR³R^{3a}, CH₂NR³SO₂NR³R^{3a}, NR³SO₂-C₁₋₄ alkyl, 20 CH₂NR³SO₂-C₁₋₄ alkyl, NR³SO₂CF₃, CH₂NR³SO₂CF₃, NR³SO₂-phenyl, CH₂NR³SO₂-phenyl, S(O)_pCF₃, CH₂S(O)_pCF₃, S(O)_p-C₁₋₄ alkyl, CH₂S(O)_p-C₁₋₄ alkyl, S(O)_p-phenyl, CH₂S(O)_p-phenyl, CF₃, and CH₂-CF₃;

R^{4c}, at each occurrence, is selected from =O, (CR³R^{3a})_rOR², 25 (CR³R^{3a})_rF, (CR³R^{3a})_rBr, (CR³R^{3a})_rCl, (CR³R^{3a})_rCF₃, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, (CR³R^{3a})_rCN, (CR³R^{3a})_rNO₂, (CR³R^{3a})_rNR²R^{2a}, (CR³R^{3a})_rN(→O)R²R^{2a}, (CR³R^{3a})_rC(O)R^{2c}, (CR³R^{3a})_rNR²C(O)R^{2b}, (CR³R^{3a})_rC(O)NR²R^{2a}, (CR³R^{3a})_rNR²C(O)NR²R^{2a}, 30 (CR³R^{3a})_rSO₂NR²R^{2a}, (CR³R^{3a})_rNR²SO₂NR²R^{2a}, (CR³R^{3a})_rNR²SO₂R^{5a}, (CR³R^{3a})_rS(O)_pR^{5a}, (CF₂)_rCF₃, (CR³R^{3a})_rC₃₋₁₀ carbocycle substituted with 0-2 R^{4b}, and

$(CR^3R^3a)_r$ 5-10 membered heterocycle substituted with 0-2 R^4b and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

5

R^5 , at each occurrence, is selected from H, =O, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, OR^3 , CH_2OR^3 , F, Cl, -CN, NO_2 , NR^3R^3a , $CH_2NR^3R^3a$, $C(O)R^3$, $CH_2C(O)R^3$, $C(O)OR^{3c}$, $CH_2C(O)OR^{3c}$, $NR^3C(O)R^3a$, $C(O)NR^3R^3a$, $NR^3C(O)NR^3R^3a$, $CH(=NOR^3d)$, $C(=NR^3)NR^3R^3a$, $NR^3C(=NR^3)NR^3R^3a$, $SO_2NR^3R^3a$, $NR^3SO_2NR^3R^3a$, $NR^3SO_2-C_{1-4}$ alkyl, $NR^3SO_2CF_3$, NR^3SO_2- phenyl, $S(O)_pCF_3$, $S(O)_p-C_{1-4}$ alkyl, $S(O)_p$ -phenyl, CF_3 , phenyl substituted with 0-2 R^6 , naphthyl substituted with 0-2 R^6 , and benzyl substituted with 0-2 R^6 ;

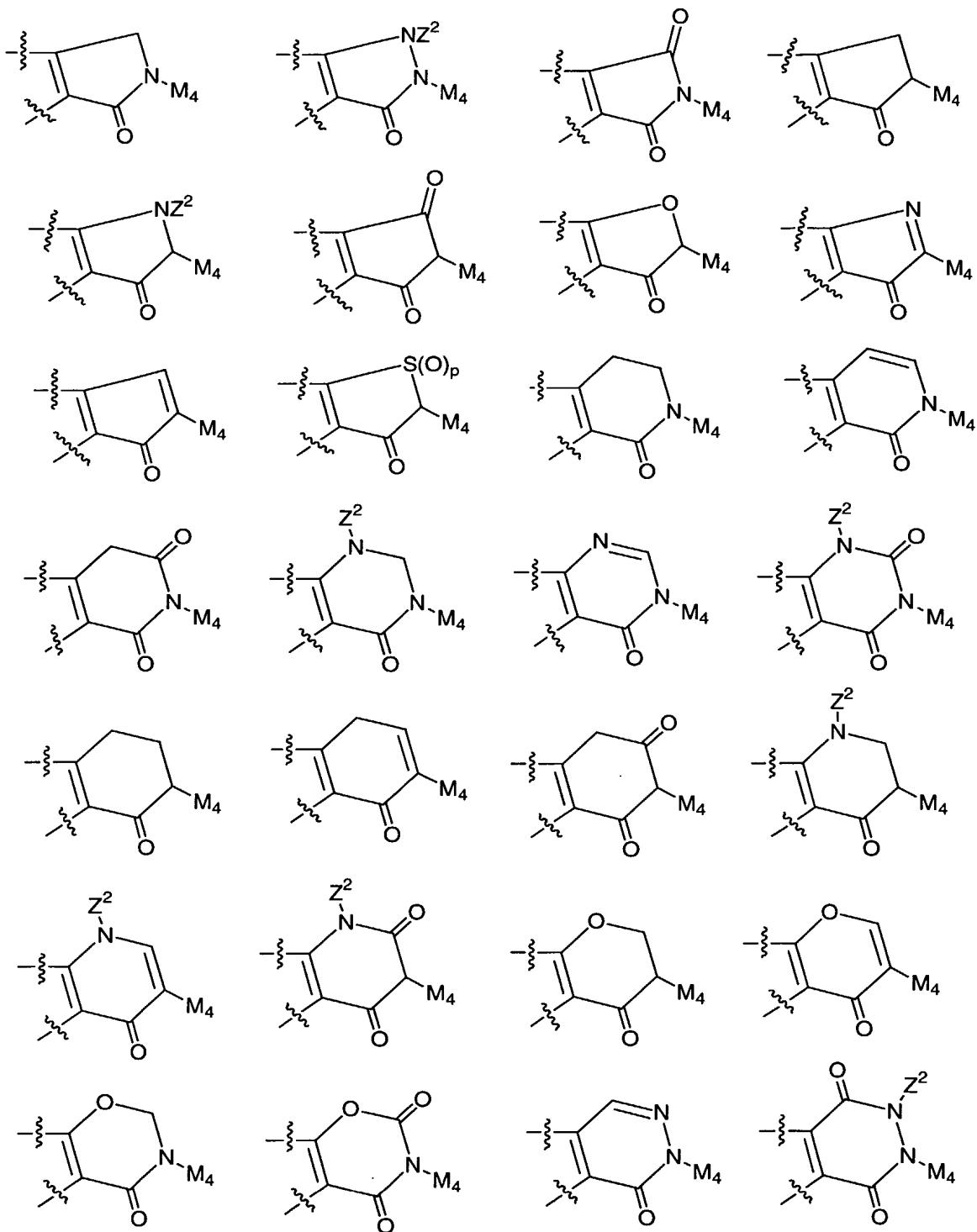
R^6 , at each occurrence, is selected from H, OH, OR^2 , F, Cl, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, -CN, NO_2 , NR^2R^{2a} , $CH_2NR^2R^{2a}$, $C(O)R^{2b}$, $CH_2C(O)R^{2b}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $C(=NH)NH_2$, $NHC(=NH)NH_2$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, and $NR^2SO_2C_{1-4}$ alkyl; and,

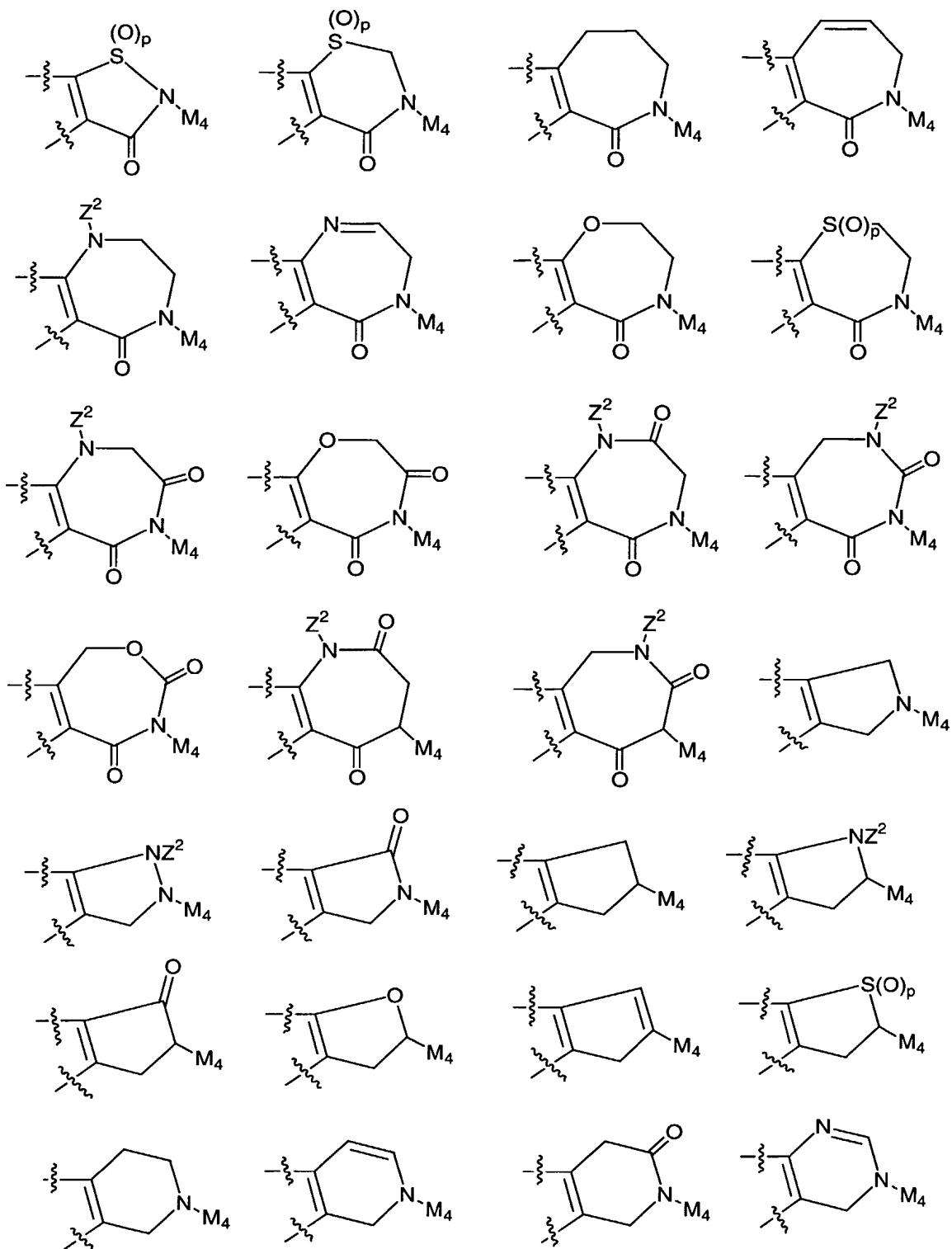
r , at each occurrence, is selected from 0, 1, 2, and 3.

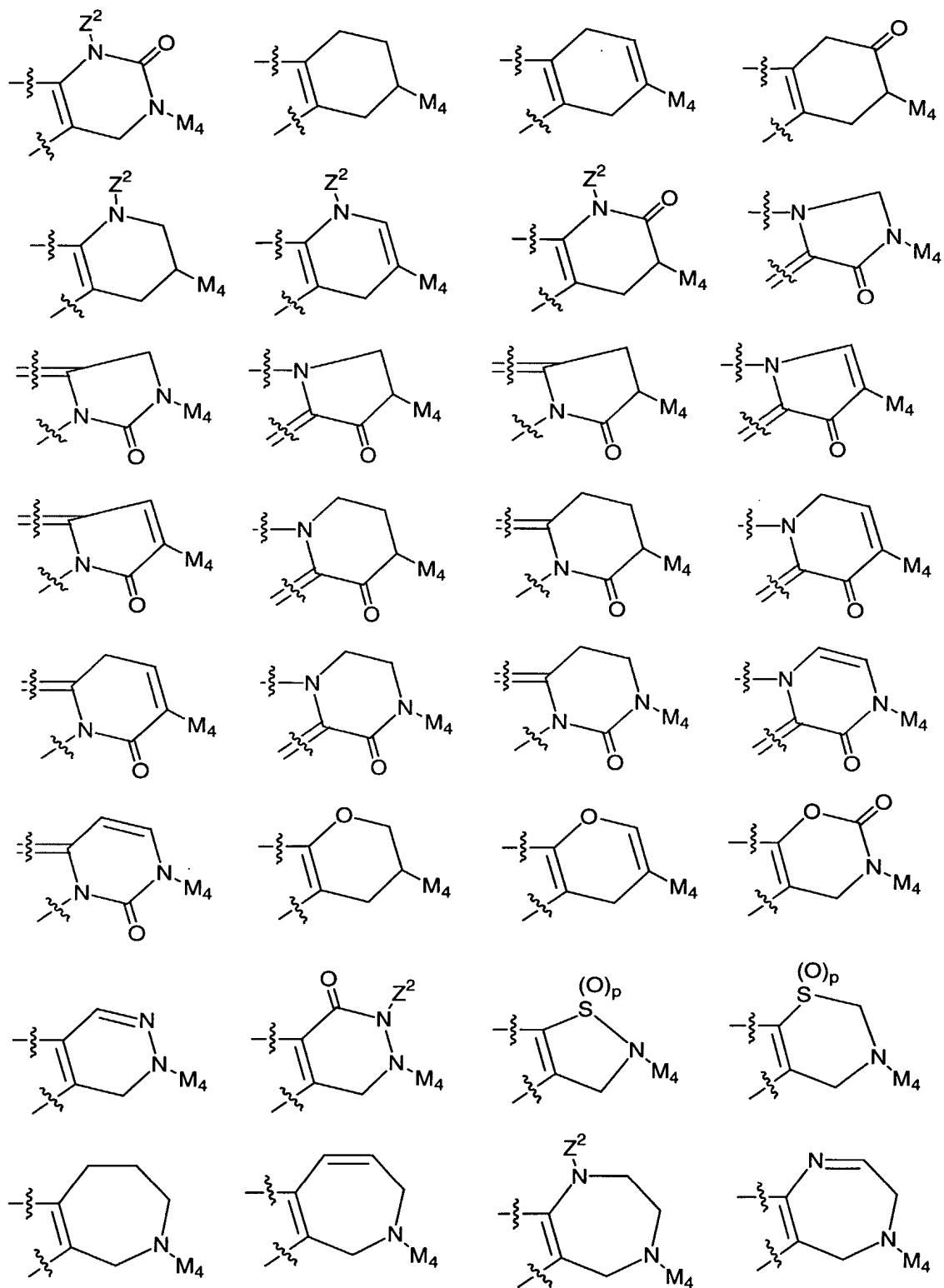
25

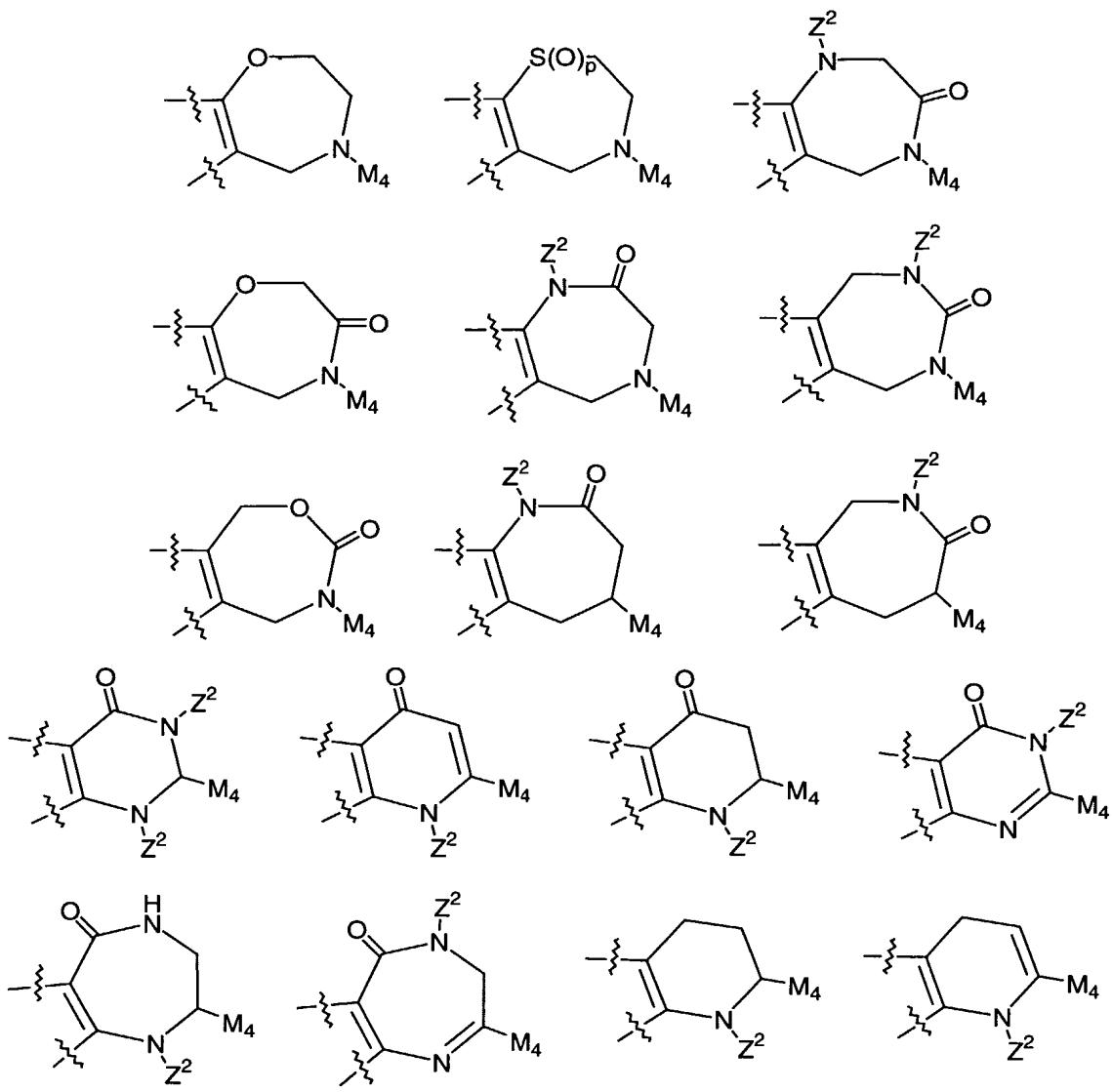
[3] In another preferred embodiment, the present invention provides a novel compound, wherein:

30 ring M is substituted with 0-2 R^{1a} and is selected from the group:

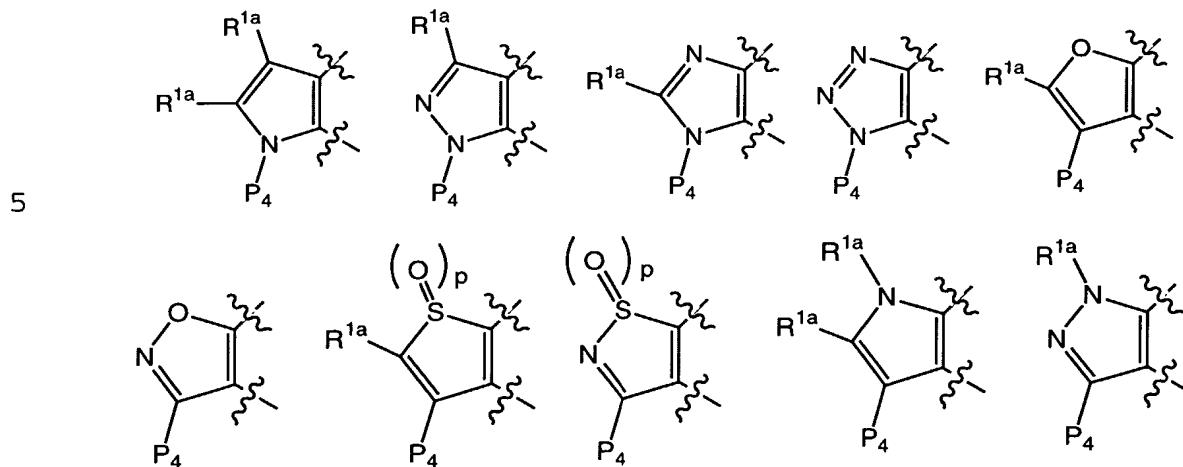


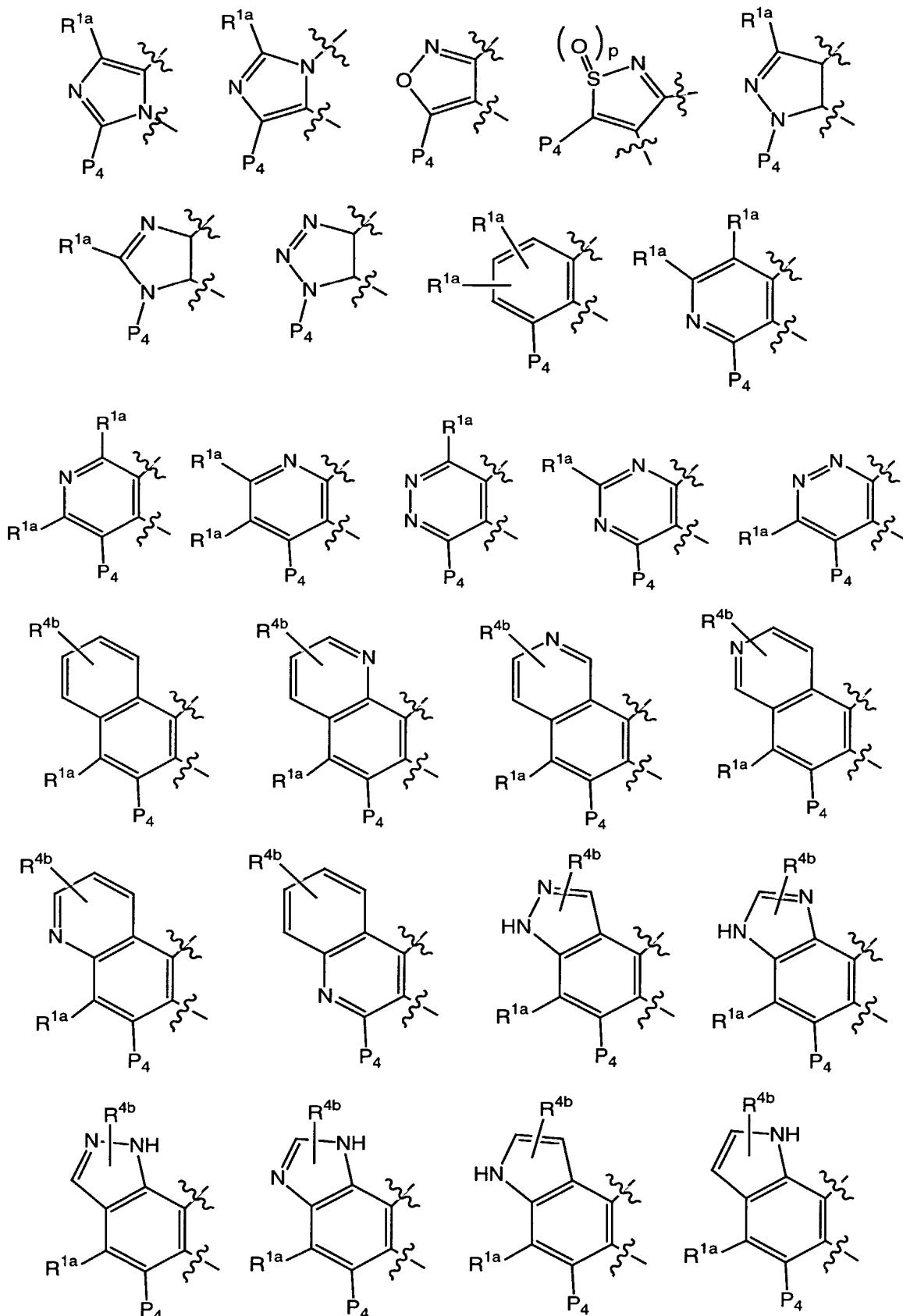


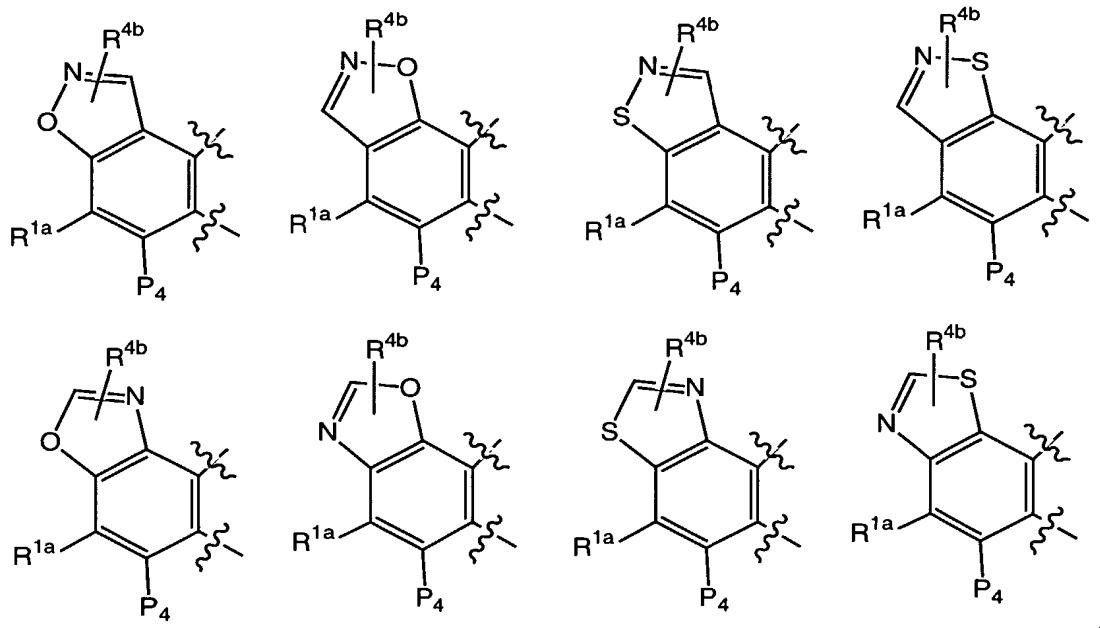




ring P, including P₁, P₂, P₃, and P₄ is selected from group:







G is selected from the group:

phenyl; 2,5-bis-aminomethyl-phenyl;

5 2-amido-4-methoxy-phenyl; 2-amido-5-chloro-phenyl;

2-amido-phenyl; 2-aminomethyl-3-fluoro-phenyl;

2-aminomethyl-3-methoxy-phenyl;

2-aminomethyl-4-fluoro-phenyl;

2-aminomethyl-4-methoxy-phenyl;

10 2-aminomethyl-5-fluoro-phenyl;

2-aminomethyl-5-methoxy-phenyl;

2-aminomethyl-6-fluoro-phenyl; 2-aminomethyl-phenyl;

2-amino-pyrid-4-yl; 2-aminosulfonyl-4-methoxy-phenyl;

2-aminosulfonyl-phenyl; 2-aminomethyl-4-ethyl-phenyl; 2-

15 aminosulfonyl-4-ethyl-phenyl; 2-amido-4-ethyl-phenyl;

2-hydroxy-4-methoxy-phenyl; 2-methylsulfonyl-phenyl;

3-(N,N-dimethylamino)-4-chloro-phenyl;

3-(N,N-dimethylamino)-phenyl; 3-(N-hydroxy-amidino)-phenyl;

3-(N-methoxy-amidino)-phenyl;

20 3-(N-methylamino)-4-chloro-phenyl;

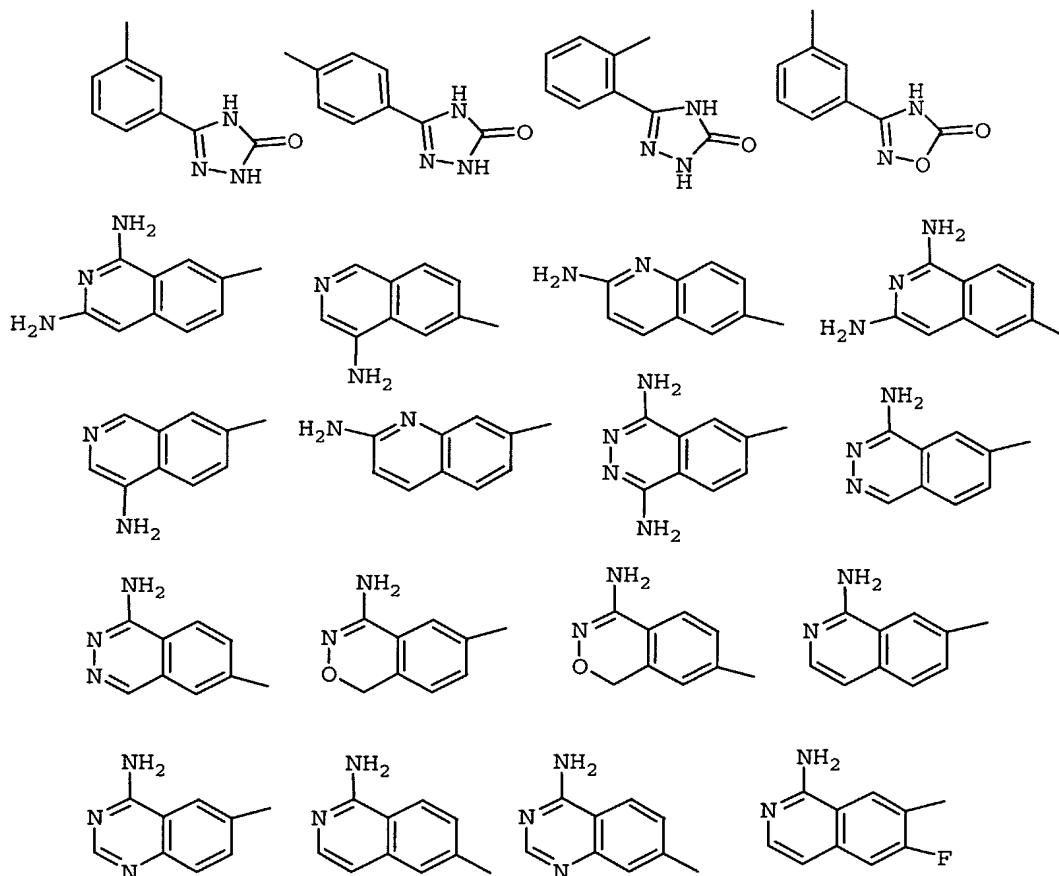
3-(N-methylamino)-phenyl; 3-amidino-phenyl;

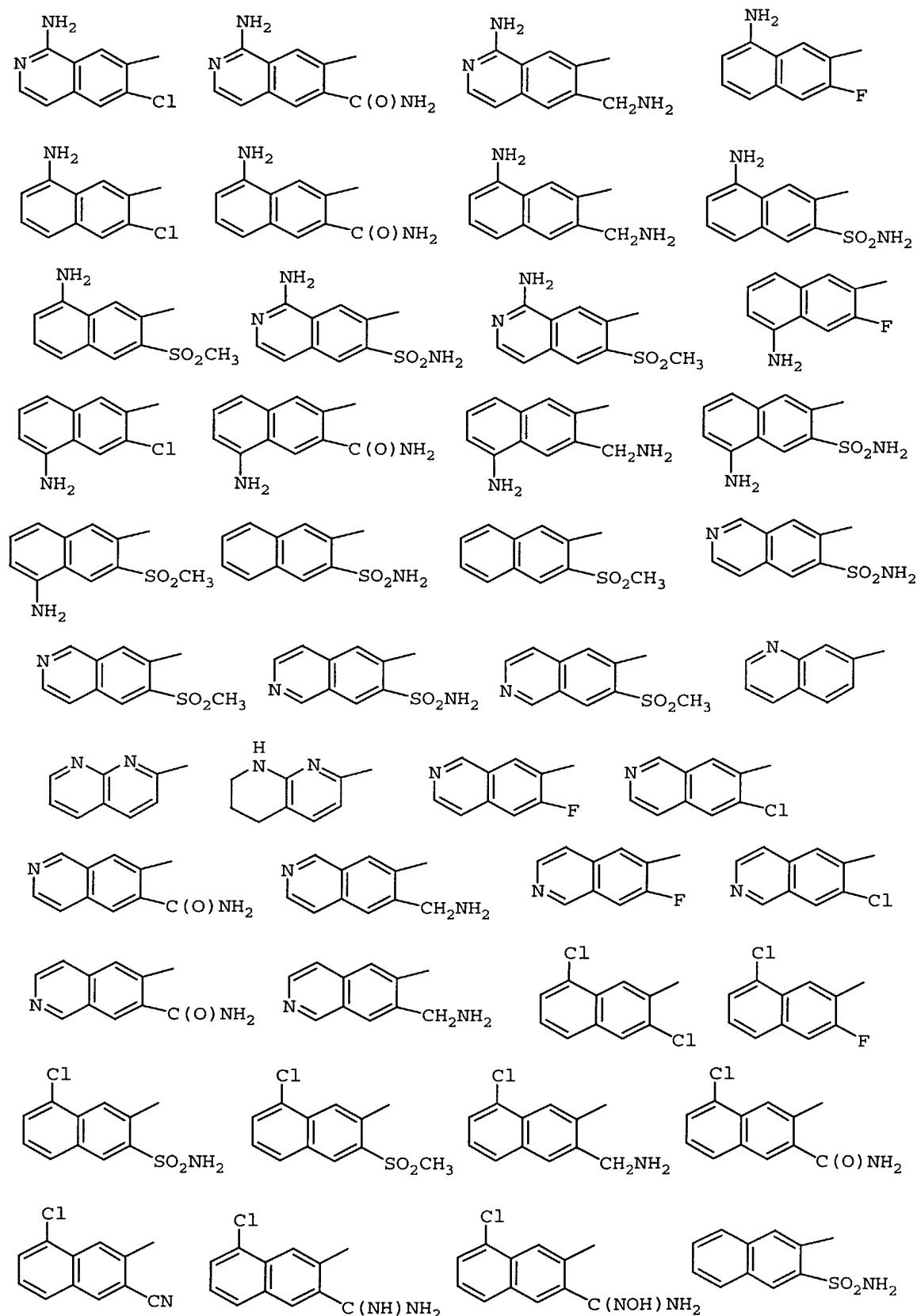
3-amido-6-hydroxy-phenyl; 3-amido-phenyl;

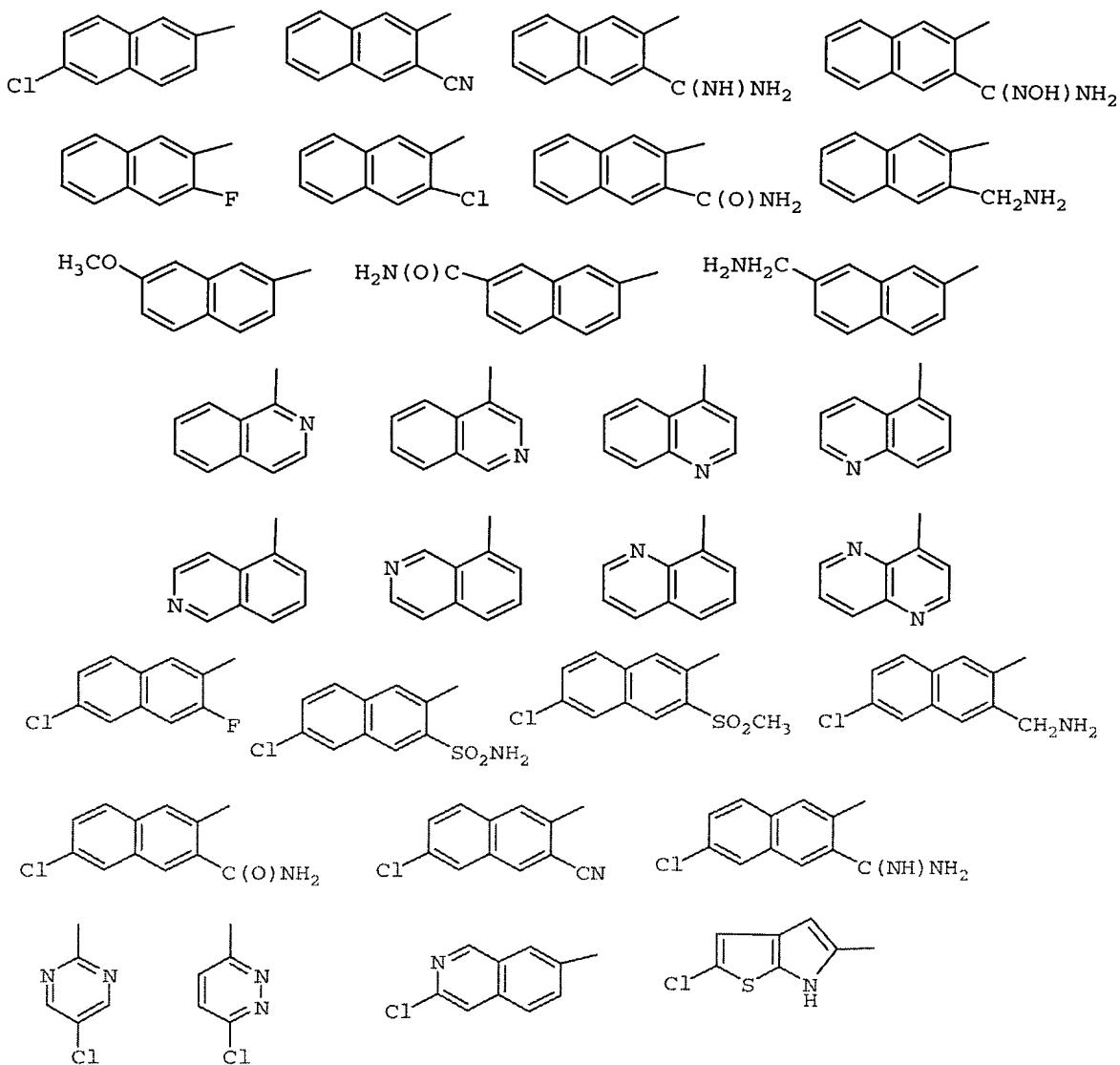
3-amino-4-chloro-phenyl; 3-aminomethyl-phenyl;

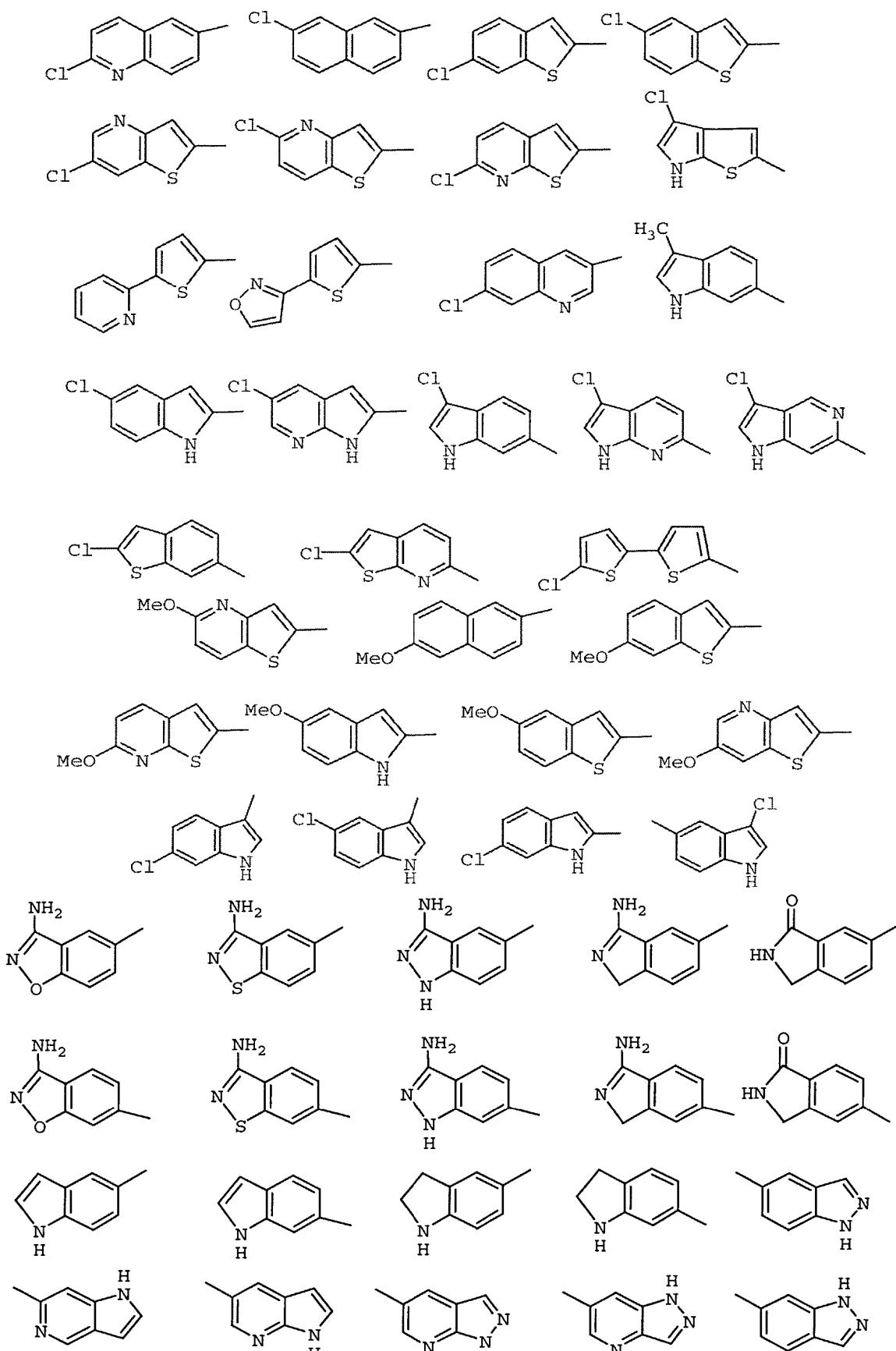
3-amino-phenyl; 3-chloro-4-fluoro-phenyl; 3-chloro-phenyl;

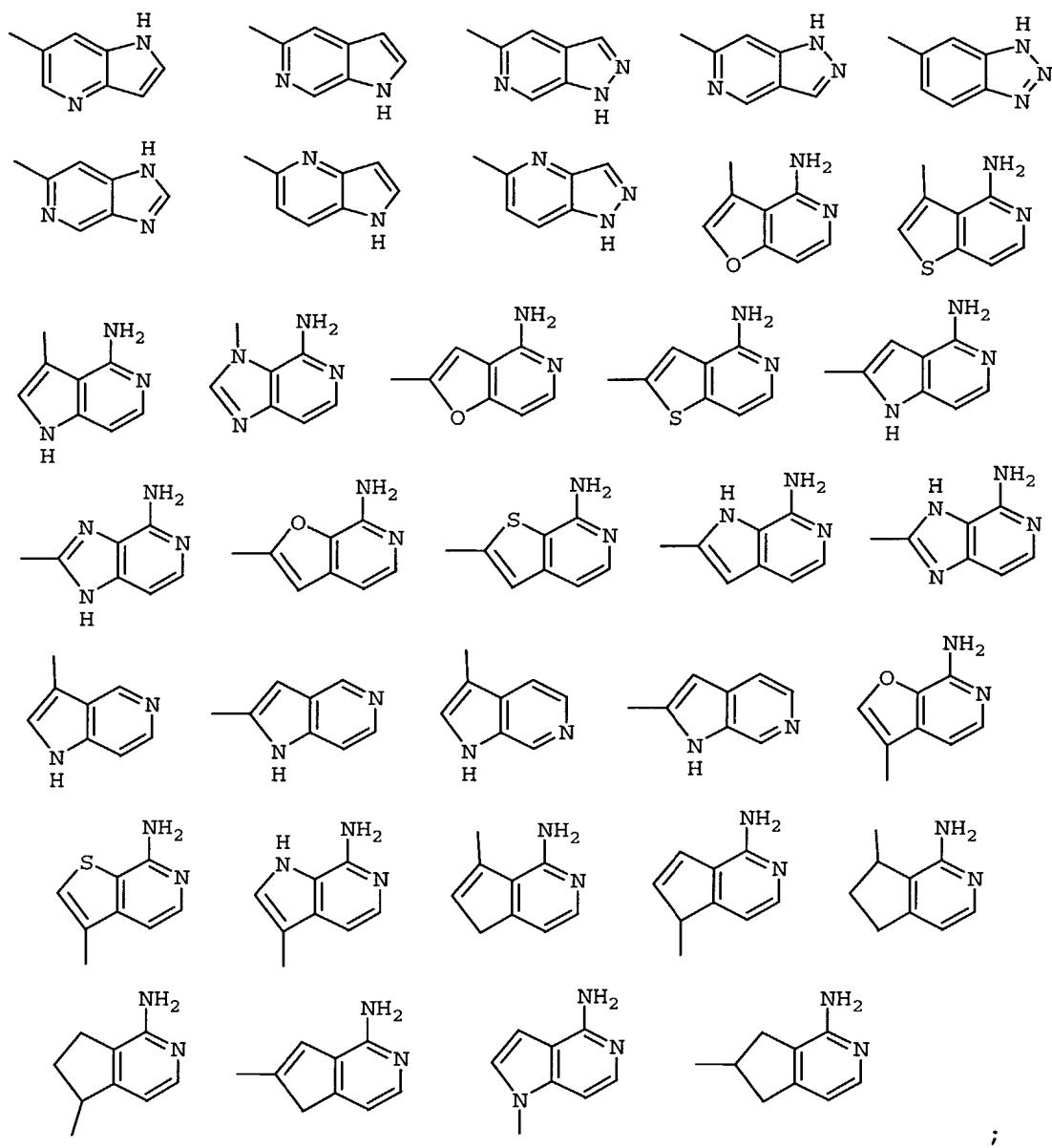
3-hydroxy-4-methoxy-phenyl;
 4-(N,N-dimethylamino)-5-chloro-thien-2-yl;
 4-(N-methylamino)-5-chloro-thien-2-yl;
 4-amino-5-chloro-thien-2-yl; 4-amino-pyrid-2-yl;
 5 4-chloro-3-fluoro-phenyl; 4-chloro-phenyl;
 4-chloro-pyrid-2-yl; 4-ethyl-phenyl; 4-ethyl-2-methylsulfonyl-phenyl; 4-ethyl-2-methoxy-phenyl;
 4-methoxy-2-methylsulfonyl-phenyl; 4-methoxy-phenyl;
 2-methoxy-pyrid-5-yl;
 10 5-(N,N-dimethylamino)-4-chloro-thien-2-yl;
 5-(N-methylamino)-4-chloro-thien-2-yl;
 5-amino-4-chloro-thien-2-yl;
 5-chloro-2-aminosulfonyl-phenyl;
 5-chloro-2-methylsulfonyl-phenyl; 5-chloro-pyrid-2-yl;
 15 5-chloro-thien-2-yl; 5-methoxy-thien-2-yl;
 5-methyl-thien-2-yl; 5-fluoro-thien-2-yl;
 6-amino-5-chloro-pyrid-2-yl; 6-amino-pyrid-2-yl;











5 G_1 is absent or is selected from $(CR^3R^{3a})_{1-3}$, $CR^3=CR^3$,
 $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uO(CR^3R^{3a})_w$,
 $(CR^3R^{3a})_uNR^{3b}(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)NR^{3b}(CR^3R^{3a})_w$,
 $(CR^3R^{3a})_uNR^{3b}C(O)(CR^3R^{3a})_w$,
 $(CR^3R^{3a})_uNR^{3b}C(O)(CR^3R^{3a})_uC(O)NR^{3b}(CR^3R^{3a})_w$,
10 $(CR^3R^{3a})_uS(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$,
 $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)NR^{3b}(CR^3R^{3a})_w$,
 $(CR^3R^{3a})_uNR^{3b}S(O)_2(CR^3R^{3a})_w$, and
 $(CR^3R^{3a})_uS(O)_2NR^{3b}(CR^3R^{3a})_w$, wherein $u + w$ total 0, 1,

or 2, provided that G₁ does not form a N-S, NCH₂N, NCH₂O, or NCH₂S bond with either group to which it is attached;

5 A is selected from one of the following carbocycles and heterocycles which are substituted with 0-2 R⁴;
cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thieryl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, 10 thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 15 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolinyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

20 X is selected from -(CR²R^{2a})₁₋₂-, -C(O)-, -S(O)₂-, -NR²S(O)₂-, -NR²S(O)₂NR²-, -NR²C(O)-, -C(O)NR²-, NR², -NR²CR²R^{2a}-, -CR²R^{2a}NR²-, O, -OCR²R^{2a}-, and -CR²R^{2a}O-;

25 Y is a C₃₋₆ monocyclic carbocycle or 5-6 membered monocyclic heterocycle, wherein the carbocycle or heterocycle consists of carbon atoms and 0-2 heteroatoms selected from N, O, and S(O)p, the carbocycle or heterocycle further comprises 0-1 double bonds and 0-1 carbonyl 30 groups, and the carbocycle or heterocycle is substituted with 0-2 R⁴;

alternatively, Y is CY¹Y², and Y¹ and Y² are independently C₁₋₂ alkyl substituted with 0-1 R⁴;

R^{1a} , at each occurrence, is selected from H, R^{1b} , $CH(CH_3)R^{1b}$, $C(CH_3)_2R^{1b}$, CH_2R^{1b} , and $CH_2CH_2R^{1b}$, provided that R^{1a} forms other than an N-halo, N-S, or N-CN bond;

5 alternatively, when two R^{1a} groups are attached to adjacent atoms or to the same carbon atom, together with the atoms to which they are attached they form a 5-6 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, 10 O, and $S(O)_p$, this ring being substituted with 0-2 R^{4b} and 0-3 ring double bonds;

R^{1b} is selected from H, CH_3 , CH_2CH_3 , F, Cl, Br, -CN, -CHO, 15 CF_3 , OR^2 , NR^2R^{2a} , $C(O)R^{2b}$, CO_2R^{2b} , $OC(O)R^2$, CO_2R^{2a} , $S(O)_pR^2$, $NR^2(CH_2)_rOR^2$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2R^2$, phenyl substituted with 0-2 R^{4b} , and 5-6 membered aromatic heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ and substituted with 0-2 20 R^{4b} , provided that R^{1b} forms other than an O-O, N-halo, N-S, or N-CN bond;

R^2 , at each occurrence, is selected from H, CF_3 , CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, phenyl substituted with 25 0-2 R^{4b} , benzyl substituted with 0-2 R^{4b} , and 5-6 membered aromatic heterocycle substituted with 0-2 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

30 R^{2a} , at each occurrence, is selected from H, CF_3 , CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, benzyl, phenyl substituted with 0-2 R^{4b} , and 5-6 membered aromatic heterocycle substituted with 0-2 R^{4b} and consisting of: carbon

atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

5 alternatively, R² and R^{2a}, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)_p;

10

R^{2b}, at each occurrence, is selected from CF₃, C₁₋₄ alkoxy, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, phenyl substituted with 0-2 R^{4b}, and 5-6 membered aromatic heterocycle substituted with 0-2 R^{4b} and consisting of: 15 carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

20 R^{2c}, at each occurrence, is selected from CF₃, OH, OCH₃, OCH₂CH₃, OCH₂CH₂CH₃, OCH(CH₃)₂, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, phenyl substituted with 0-2 R^{4b}, and 5-6 membered aromatic heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

25

R^{2d}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, C₃₋₆ carbocycle substituted with 0-2 R^{4c}, -(CR³R^{3a})-C₃₋₆ carbocycle substituted with 0-2 R^{4c}, 5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: 30 carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, and -(CR³R^{3a})-5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group

consisting of N, O, and S(O)_p, provided that R^{2d} forms other than a N-halo, N-C-halo, S(O)_p-halo, O-halo, N-S, S-N, S(O)_p-S(O)_p, S-O, O-N, O-S, or O-O moiety;

5 R^{2e}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, C₃₋₆ carbocycle substituted with 0-2 R^{4c}, -(CR³R^{3a})-C₃₋₆ carbocycle substituted with 0-2 R^{4c}, 5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, and -(CR³R^{3a})-5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2e} forms other than a C(O)-halo or C(O)-S(O)_p moiety;

10

15

R⁴, at each occurrence, is selected from H, (CH₂)₂OR², CH₂OR², OR², F, Cl, Br, I, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂CH₂CH₂CH₃, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, C(CH₃)₃, -CN, NO₂, NR²R^{2a}, CH₂NR²R^{2a}, (CH₂)₂NR²R^{2a}, 20 C(O)R^{2c}, NR²C(O)R^{2b}, C(O)NR²R^{2a}, SO₂NR²R^{2a}, CF₃, and CF₂CF₃;

R^{4a} is selected from -(CR³R^{3g})_r-5-6 membered carbocycle 25 substituted with 0-3 R^{4c}, -(CR³R^{3g})_r-5-6 membered heterocycle substituted with 0-3 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, (CR³R^{3g})_rNR^{2d}R^{2d}, (CR³R^{3g})_rN(→O)R^{2d}R^{2d}, (CR³R^{3g})_rOR^{2d}, (CR³R^{3g})_r-NR^{2d}C(O)R^{2e}, (CR³R^{3g})_r-C(O)R^{2e}, 30 (CR³R^{3g})_r-OC(O)R^{2e}, (CR³R^{3g})_r-C(O)NR^{2d}R^{2d}, (CR³R^{3g})_r-C(O)OR^{2d}, (CR³R^{3g})_r-NR^{2d}C(O)NR^{2d}R^{2d}, (CR³R^{3g})_r-NR^{2d}C(O)OR^{2d}, (CR³R^{3g})_r-SO₂NR^{2d}R^{2d},

$(CR^3R^3g)_r-NR^{2d}SO_2R^{2d}$, and $(CR^3R^3g)_r-S(O)_pR^{2d}$, provided that $S(O)_pR^{2d}$ forms other than $S(O)_2H$ or $S(O)H$;

5 R^{4b} , at each occurrence, is selected from H, =O, OR³, CH₂OR³, F, Cl, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, -CN, NO₂, NR³R^{3a}, CH₂NR³R^{3a}, C(O)R³, CH₂-C(O)R³, C(O)OR^{3c}, CH₂-C(O)OR^{3c}, NR³C(O)R^{3a}, CH₂NR³C(O)R^{3a}, C(O)NR³R^{3a}, CH₂-C(O)NR³R^{3a}, SO₂NR³R^{3a}, CH₂SO₂NR³R^{3a}, NR³SO₂-C₁₋₄ alkyl, CH₂NR³SO₂-C₁₋₄ alkyl, NR³SO₂-phenyl, CH₂NR³SO₂-phenyl, 10 S(O)_pCF₃, CH₂S(O)_pCF₃, S(O)_p-C₁₋₄ alkyl, CH₂S(O)_p-C₁₋₄ alkyl, S(O)_p-phenyl, CH₂S(O)_p-phenyl, and CF₃;

15 R^{4c} , at each occurrence, is selected from =O, OR², (CR³R^{3a})OR², F, (CR³R^{3a})F, Br, (CR³R^{3a})Br, Cl, (CR³R^{3a})Cl, CF₃, (CR³R^{3a})CF₃, C₁₋₄ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, -CN, (CR³R^{3a})CN, NO₂, (CR³R^{3a})NO₂, NR²R^{2a}, (CR³R^{3a})NR²R^{2a}, N(→O)R²R^{2a}, (CR³R^{3a})N(→O)R²R^{2a}, C(O)R^{2c}, (CR³R^{3a})C(O)R^{2c}, NR²C(O)R^{2b}, (CR³R^{3a})NR²C(O)R^{2b}, 20 C(O)NR²R^{2a}, (CR³R^{3a})C(O)NR²R^{2a}, NR²C(O)NR²R^{2a}, (CR³R^{3a})NR²C(O)NR²R^{2a}, SO₂NR²R^{2a}, (CR³R^{3a})SO₂NR²R^{2a}, NR²SO₂NR²R^{2a}, (CR³R^{3a})NR²SO₂NR²R^{2a}, NR²SO₂R^{5a}, (CR³R^{3a})NR²SO₂R^{5a}, S(O)_pR^{5a}, (CR³R^{3a})S(O)_pR^{5a}, CF₃, CF₂CF₃, C₃₋₁₀ carbocycle substituted with 0-2 R^{4b}, 25 (CR³R^{3a})-C₃₋₁₀ carbocycle substituted with 0-2 R^{4b}, 5-10 membered heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, and (CR³R^{3a})-5-10 membered heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^5 , at each occurrence, is selected from H, =O, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, OR^3 , CH_2OR^3 , F, Cl, -CN, NO_2 , NR^3R^{3a} , $CH_2NR^3R^{3a}$, $C(O)R^3$, $CH_2C(O)R^3$, $C(O)OR^{3c}$, $CH_2C(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$,

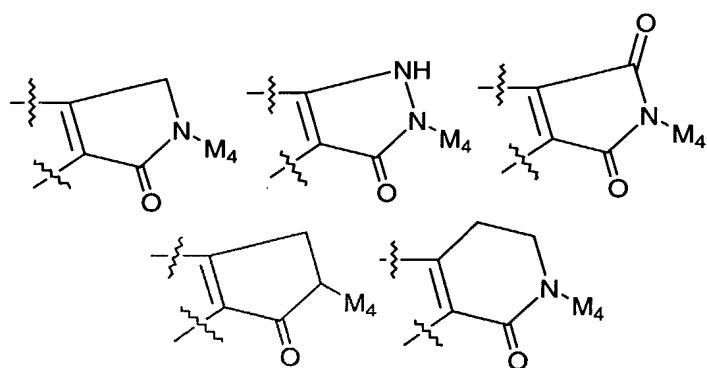
5 $NR^3SO_2-C_1-4$ alkyl, $NR^3SO_2CF_3$, NR^3SO_2 -phenyl, $S(O)_pCF_3$, $S(O)_p-C_1-4$ alkyl, $S(O)_p$ -phenyl, CF_3 , phenyl substituted with 0-2 R^6 , naphthyl substituted with 0-2 R^6 , and benzyl substituted with 0-2 R^6 ; and,

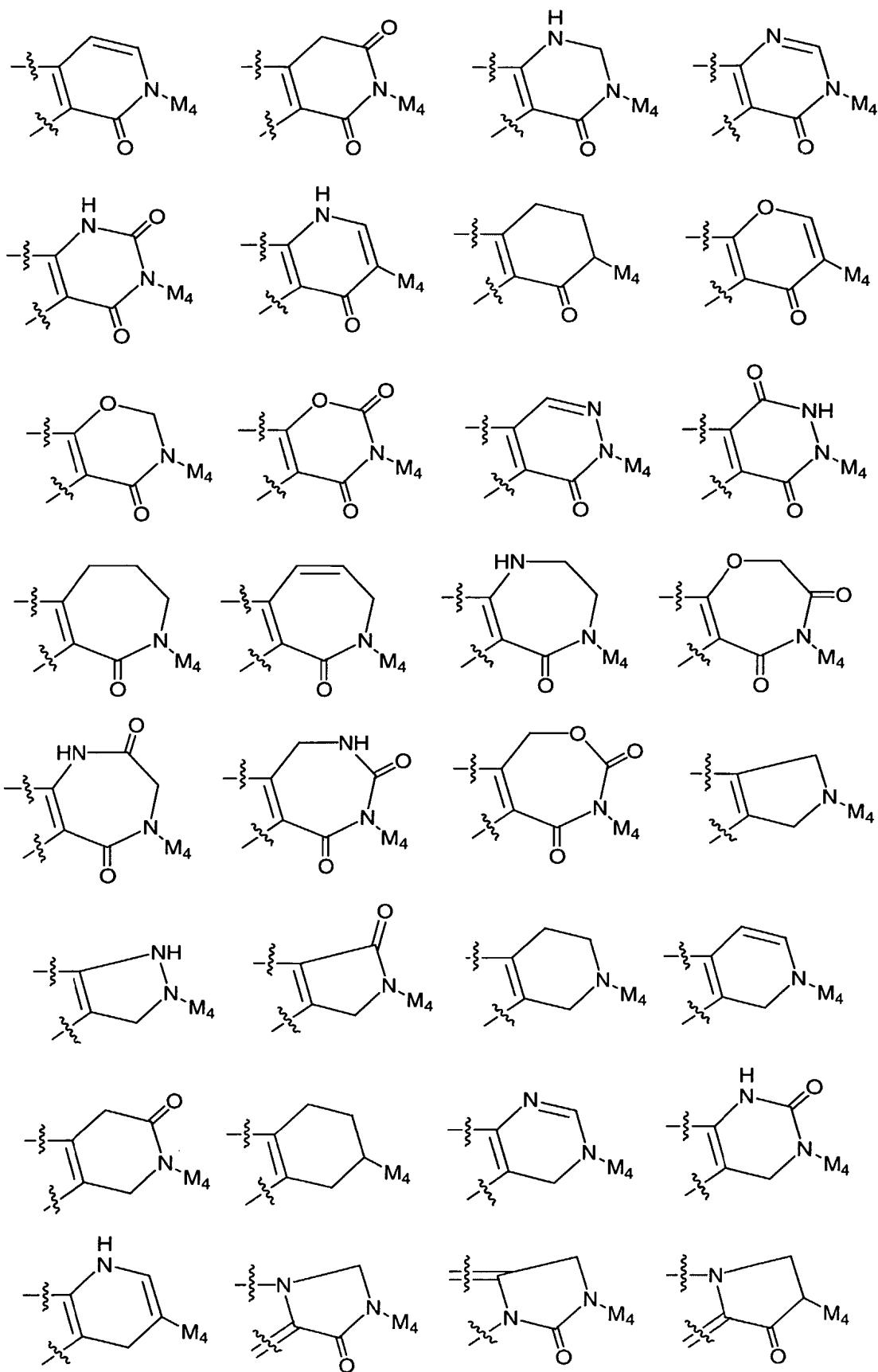
10 R^6 , at each occurrence, is selected from H, OH, OR^2 , F, Cl, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, -CN, NO_2 , NR^2R^{2a} , $CH_2NR^2R^{2a}$, $C(O)R^{2b}$, $CH_2C(O)R^{2b}$, $NR^2C(O)R^{2b}$, $SO_2NR^2R^{2a}$, and $NR^2SO_2C_1-4$ alkyl.

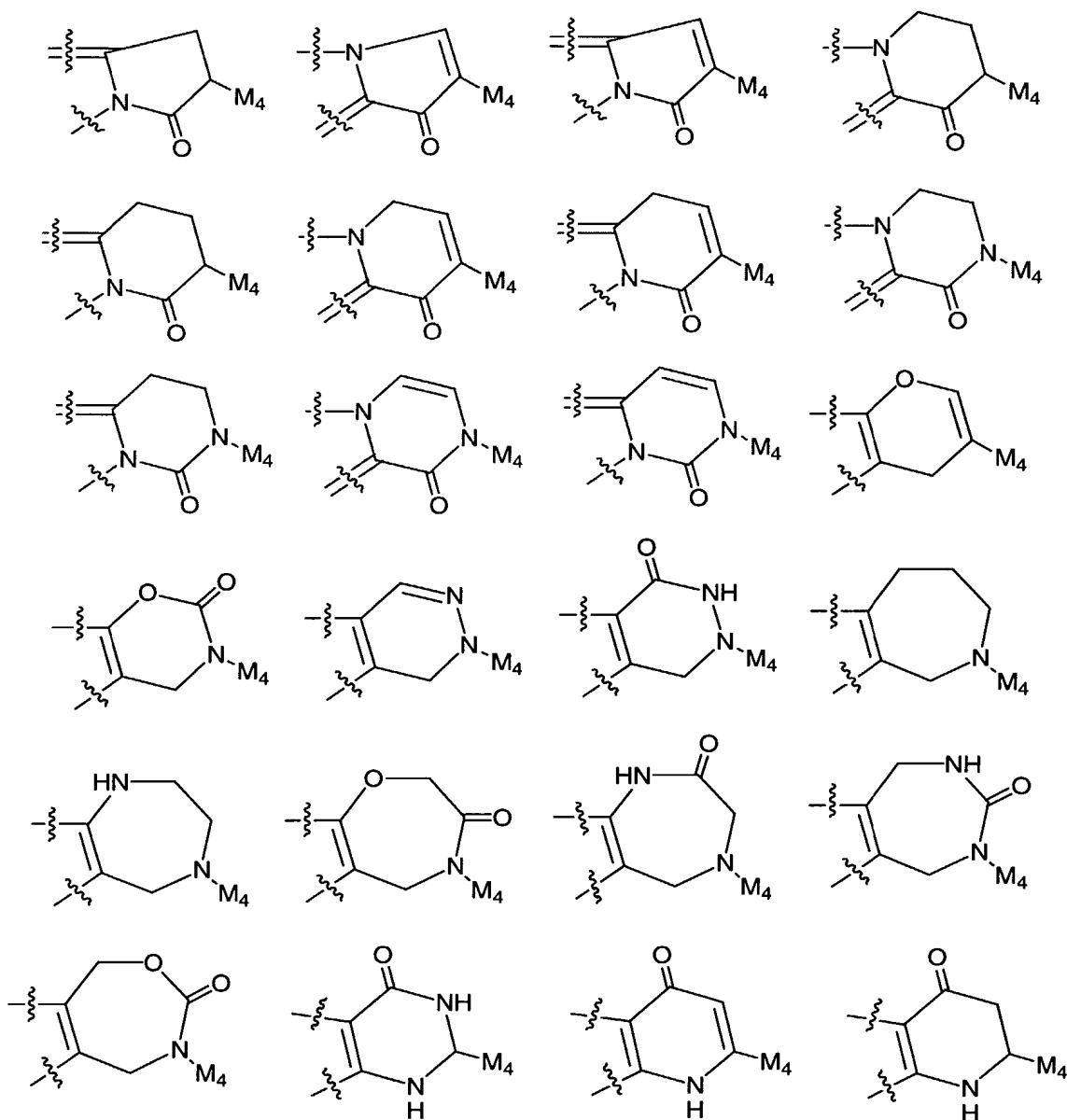
15

[4] In another preferred embodiment, the present invention provides a novel compound, wherein:

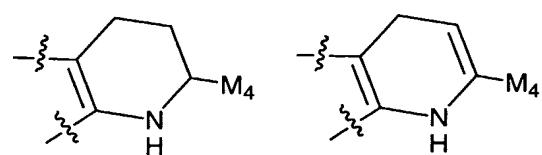
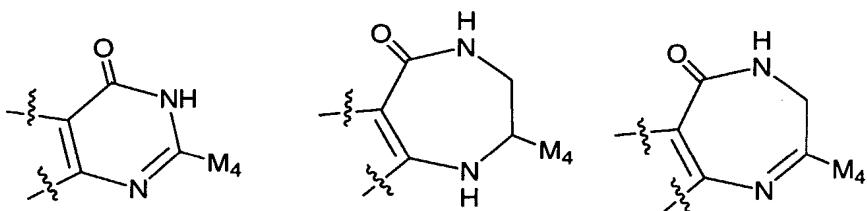
ring M is substituted with 0-2 R^{1a} and is selected from the
20 group:



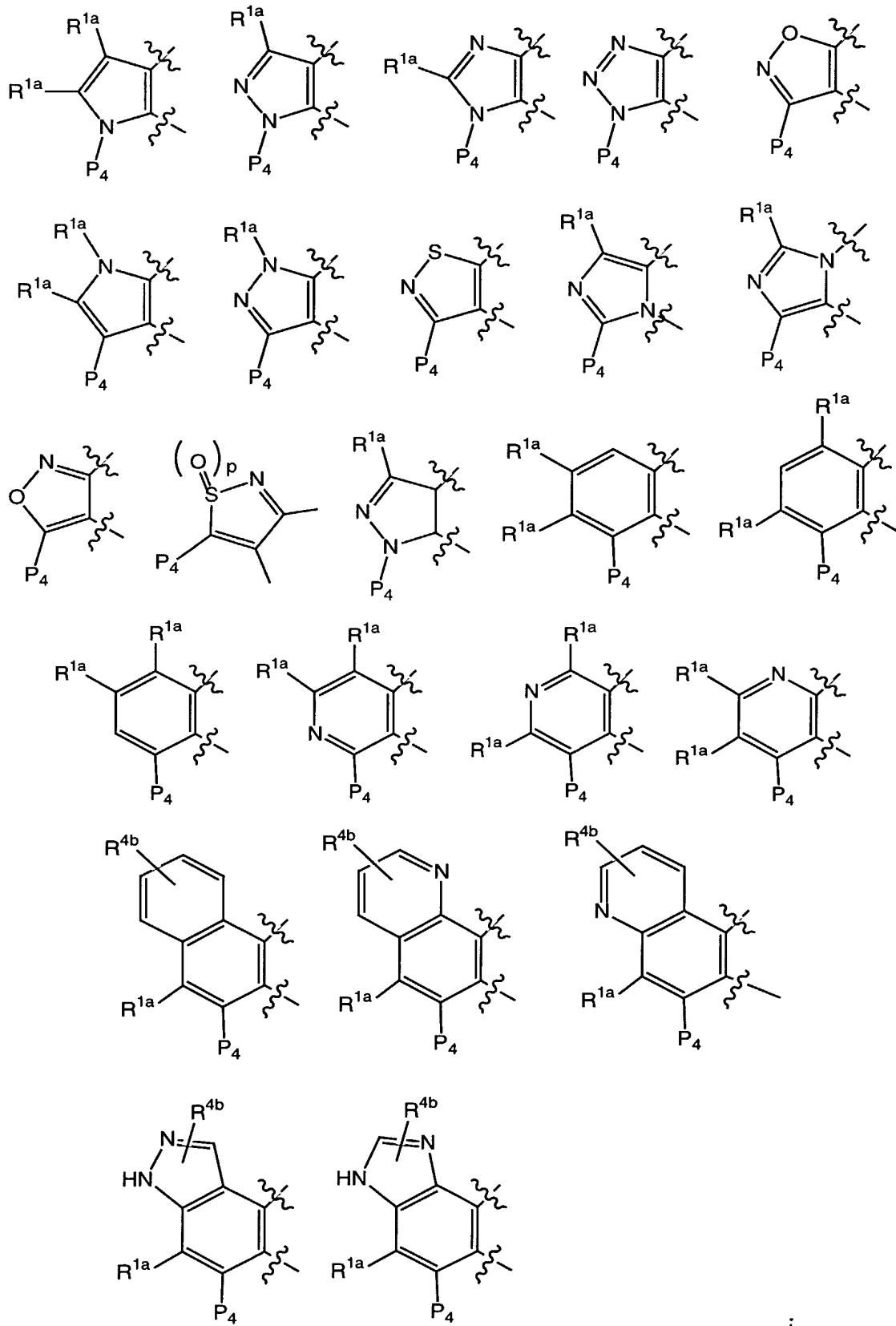




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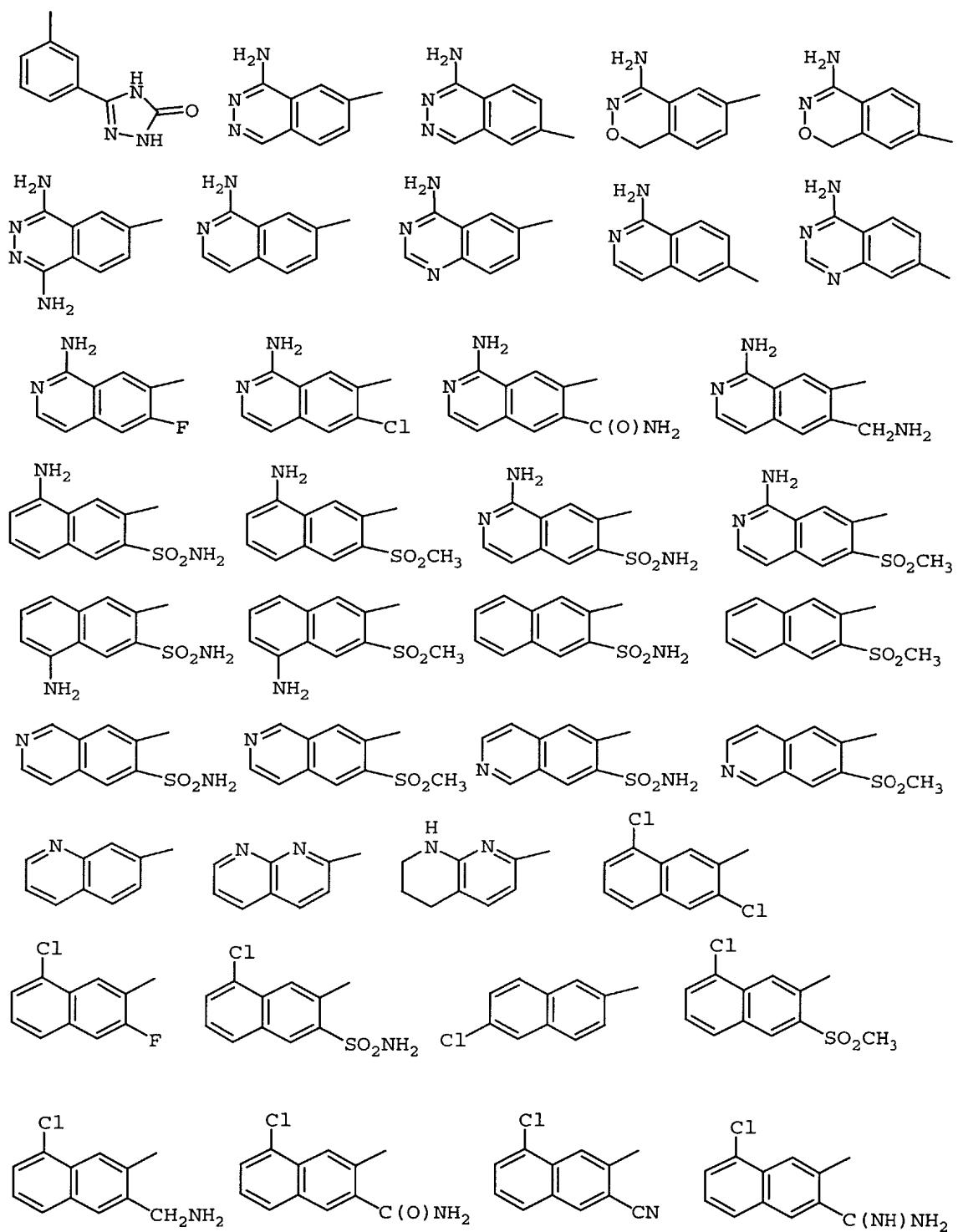
ring P, including P₁, P₂, P₃, and P₄ is selected from group:

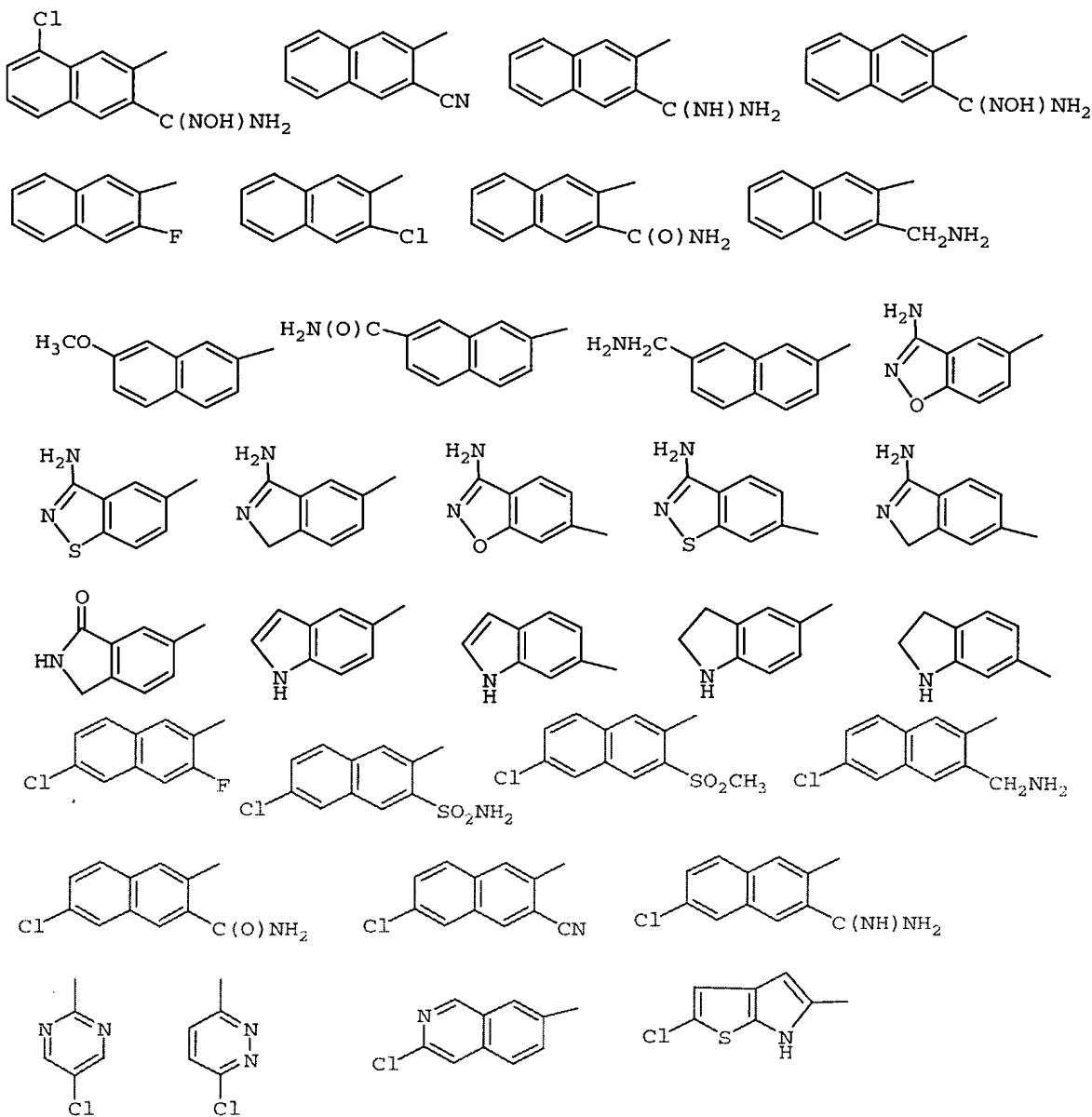


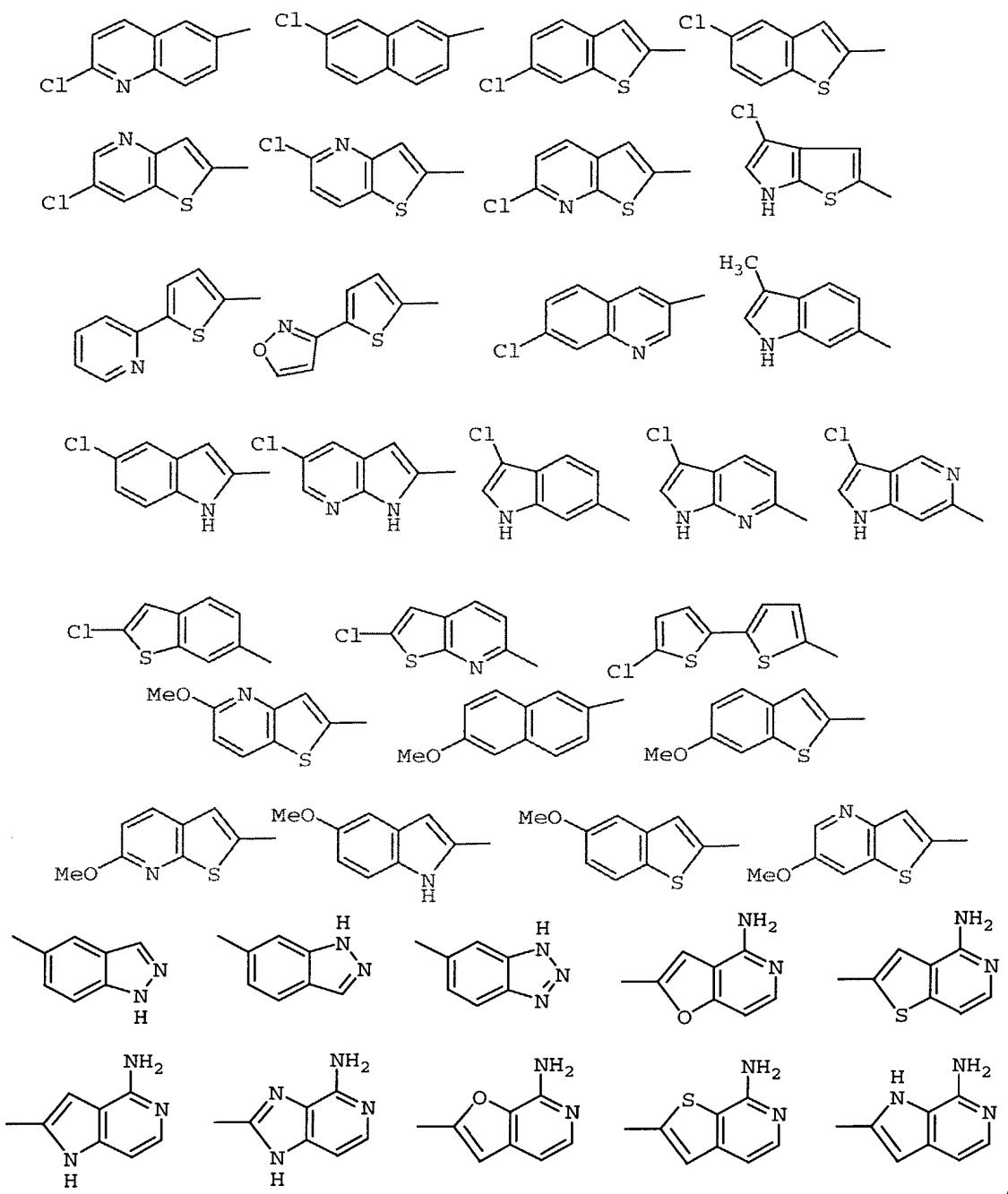
;

G is selected from the group:

phenyl; 2-amido-4-methoxy-phenyl; 2-amido-phenyl;
2-aminomethyl-3-fluoro-phenyl;
5 2-aminomethyl-4-fluoro-phenyl;
2-aminomethyl-4-methoxy-phenyl;
2-aminomethyl-5-fluoro-phenyl;
2-aminomethyl-5-methoxy-phenyl;
2-aminomethyl-6-fluoro-phenyl; 2-aminomethyl-phenyl;
10 2-amino-pyrid-4-yl; 2-aminosulfonyl-4-methoxy-phenyl;
2-aminosulfonyl-phenyl; 2-methylsulfonyl-phenyl; 2-
aminomethyl-4-ethyl-phenyl; 2-aminosulfonyl-4-ethyl-phenyl;
2-amido-4-ethyl-phenyl;
3-(N,N-dimethylamino)-4-chloro-phenyl;
15 3-(N,N-dimethylamino)-phenyl;
3-(N-methylamino)-4-chloro-phenyl;
3-(N-methylamino)-phenyl; 3-amido-phenyl;
3-amino-4-chloro-phenyl; 3-aminomethyl-phenyl;
3-amino-phenyl; 3-chloro-phenyl;
20 4-(N,N-dimethylamino)-5-chloro-thien-2-yl;
4-(N-methylamino)-5-chloro-thien-2-yl;
4-amino-5-chloro-thien-2-yl; 4-chloro-phenyl; 4-ethyl-
phenyl; 4-ethyl-2-methylsulfonyl-phenyl; 4-ethyl-2-methoxy-
phenyl; 4-methoxy-2-methylsulfonyl-phenyl;
25 4-methoxy-phenyl;
5-(N,N-dimethylamino)-4-chloro-thien-2-yl;
5-(N-methylamino)-4-chloro-thien-2-yl;
5-amino-4-chloro-thien-2-yl; 5-chloro-pyrid-2-yl;
5-chloro-thien-2-yl; 5-methoxy-thien-2-yl;
30 5-methyl-thien-2-yl; 5-fluoro-thien-2-yl;
6-amino-5-chloro-pyrid-2-yl; 6-amino-pyrid-2-yl;







5 G_1 is absent or is selected from CH_2 , CH_2CH_2 , $\text{CH}=\text{CH}$, CH_2O , OCH_2 , NH , CH_2NH , NHCH_2 , $\text{CH}_2\text{C}(\text{O})$, $\text{C}(\text{O})\text{CH}_2$, $\text{C}(\text{O})\text{NH}$, $\text{NHC}(\text{O})$, $\text{CH}_2\text{S}(\text{O})_2$, $\text{S}(\text{O})_2(\text{CH}_2)$, SO_2NH , and NHSO_2 , provided that G_1 does not form a N-S , NCH_2N , NCH_2O , or NCH_2S bond with either group to which it is attached;

A is selected from cyclohexyl, piperidinyl, phenyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R⁴;

5 X is selected from CH₂, C(O), -S(O)₂-, -NHC(O)-, -C(O)NH-, -CH₂NH-, O, and -CH₂O-;

Y is selected from C(CH₃)₂, C(CH₂CH₃)₂, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentanonyl, cyclohexyl, cyclohexanonyl, pyrrolidinyl, pyrrolidinonyl, 10 piperidinyl, piperidinonyl, tetrahydrofuranyl, and tetrahydropyranyl, and, when Y is a ring, Y is substituted with 0-1 R⁴;

15 R^{1a}, at each occurrence, is selected from H, R^{1b}, CH(CH₃)R^{1b}, C(CH₃)₂R^{1b}, and CH₂R^{1b}, provided that R^{1a} forms other than an N-halo, N-S, or N-CN bond;

20 R^{1b} is selected from CH₃, CH₂CH₃, F, Cl, Br, -CN, CF₃, OR², NR²R^{2a}, C(O)R^{2b}, CO₂R^{2b}, CO₂R^{2a}, S(O)_pR², C(O)NR²R^{2a}, SO₂NR²R^{2a}, NR²SO₂R², and 5-6 membered aromatic heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p and substituted with 0-2 R^{4b}, provided 25 that R^{1b} forms other than an O-O, N-halo, N-S, or N-CN bond;

30 R², at each occurrence, is selected from H, CH₃, CH₂CH₃, CH(CH₃)₂, phenyl substituted with 0-1 R^{4b}, benzyl substituted with 0-1 R^{4b}, and 5-6 membered aromatic heterocycle substituted with 0-1 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2a}, at each occurrence, is selected from H, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, phenyl substituted with 0-1 R^{4b}, and 5-6 membered aromatic heterocycle substituted with 0-1 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

alternatively, R² and R^{2a}, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-1 R^{4b} and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2b}, at each occurrence, is selected from OH, OCH₃, OCH₂CH₃, OCH₂CH₂CH₃, OCH(CH₃)₂, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, phenyl substituted with 0-1 R^{4b}, and 5-6 membered aromatic heterocycle substituted with 0-1 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2c}, at each occurrence, is selected from OH, OCH₃, OCH₂CH₃, OCH₂CH₂CH₃, OCH(CH₃)₂, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, benzyl, phenyl substituted with 0-1 R^{4b}, and 5-6 membered aromatic heterocycle substituted with 0-1 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

R^{2d}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, C₃₋₆ carbocycle substituted with 0-2 R^{4c}, -(CH₂)-C₃₋₆ carbocycle substituted with 0-2 R^{4c}, 5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4

heteroatoms selected from the group consisting of N, O, and S(O)_p, and -(CH₂)-5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2d} forms other than a N-halo, N-C-halo, S(O)_p-halo, O-halo, N-S, S-N, S(O)_p-S(O)_p, S-O, O-N, O-S, or O-O moiety;

10 R^{2e}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, C₃₋₆ carbocycle substituted with 0-2 R^{4c}, -(CH₂)-C₃₋₆ carbocycle substituted with 0-2 R^{4c}, 5-6 membered heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, and -(CH₂)-5-6 membered heterocycle and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2e} forms other than a C(O)-halo or C(O)-S(O)_p moiety;

20 R⁴, at each occurrence, is selected from OH, OR², CH₂OR², (CH₂)₂OR², F, Br, Cl, I, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, CH₂CH₂CH₂CH₃, CH₂CH(CH₃)₂, CH(CH₃)CH₂CH₃, C(CH₃)₃, NR²R^{2a}, CH₂NR²R^{2a}, (CH₂)₂NR²R^{2a}, CF₃, and CF₂CF₃;

30 R^{4a} is selected from -(CR³R^{3g})_r-5-6 membered carbocycle substituted with 0-3 R^{4c}, -(CR³R^{3g})_r-5-6 membered heterocycle substituted with 0-3 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, (CR³R^{3g})_rNR^{2d}R^{2d}, (CR³R^{3g})_rN(→O)R^{2d}R^{2d}, (CR³R^{3g})_rOR^{2d}, (CR³R^{3g})_r-C(O)NR^{2d}R^{2d}, (CR³R^{3g})_r-NR^{2d}C(O)R^{2e},

$(CR^3R^3g)_r-C(O)R^{2e}$, $(CR^3R^3g)_r-NR^{2d}C(O)NR^{2d}R^{2d}$,
 $(CR^3R^3g)_r-NR^{2d}C(O)OR^{2d}$, $(CR^3R^3g)_r-NR^{2d}SO_2R^{2d}$, and
 $(CR^3R^3g)_r-S(O)_pR^{2d}$, provided that $S(O)_pR^{2d}$ forms other
than $S(O)_2H$ or $S(O)H$;

5

R^{4b} , at each occurrence, is selected from H , $=O$, OR^3 ,
 CH_2OR^3 , F , Cl , CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $-CN$,
 NO_2 , NR^3R^{3a} , $CH_2NR^3R^{3a}$, $C(O)R^3$, $C(O)OR^{3c}$, $NR^3C(O)R^{3a}$,
 $C(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2-C_{1-4}$ alkyl, NR^3SO_2 -phenyl,
10 $S(O)_p-C_{1-4}$ alkyl, $S(O)_p$ -phenyl, and CF_3 ;

R^{4c} , at each occurrence, is selected from $=O$, OR^2 , CH_2OR^2 ,
 F , Br , Cl , CF_3 , CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, C_{2-3}
alkenyl, C_{2-3} alkynyl, $-CN$, NO_2 , NR^2R^{2a} , $CH_2NR^2R^{2a}$,

15 $N(\rightarrow O)R^2R^{2a}$, $CH_2N(\rightarrow O)R^2R^{2a}$, $C(O)R^{2c}$, $CH_2C(O)R^{2c}$,
 $NR^2C(O)R^{2b}$, $CH_2NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $CH_2C(O)NR^2R^{2a}$,
 $SO_2NR^2R^{2a}$, $CH_2SO_2NR^2R^{2a}$, $NR^2SO_2R^{5a}$, $CH_2NR^2SO_2R^{5a}$,
 $S(O)_pR^{5a}$, $CH_2S(O)_pR^{5a}$, CF_3 , CF_2CF_3 , C_{3-6} carbocycle
substituted with 0-2 R^{4b} , $(CH_2)-C_{3-6}$ carbocycle
20 substituted with 0-2 R^{4b} , 5-6 membered heterocycle
substituted with 0-2 R^{4b} and consisting of carbon atoms
and from 1-4 heteroatoms selected from the group
consisting of N , O , and $S(O)_p$, and $(CH_2)-5-6$ membered
heterocycle substituted with 0-2 R^{4b} and consisting of
25 carbon atoms and from 1-4 heteroatoms selected from
the group consisting of N , O , and $S(O)_p$;

R^5 , at each occurrence, is selected from H , $=O$, CH_3 , CH_2CH_3 ,
 $CH_2CH_2CH_3$, $CH(CH_3)_2$, OR^3 , CH_2OR^3 , F , Cl , $-CN$, NO_2 ,
30 NR^3R^{3a} , $CH_2NR^3R^{3a}$, $C(O)R^3$, $C(O)OR^{3c}$, $NR^3C(O)R^{3a}$,
 $C(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2-C_{1-4}$ alkyl, NR^3SO_2 -phenyl,
 $S(O)_p-C_{1-4}$ alkyl, $S(O)_p$ -phenyl, CF_3 , phenyl substituted

with 0-2 R⁶, naphthyl substituted with 0-2 R⁶, and benzyl substituted with 0-2 R⁶;

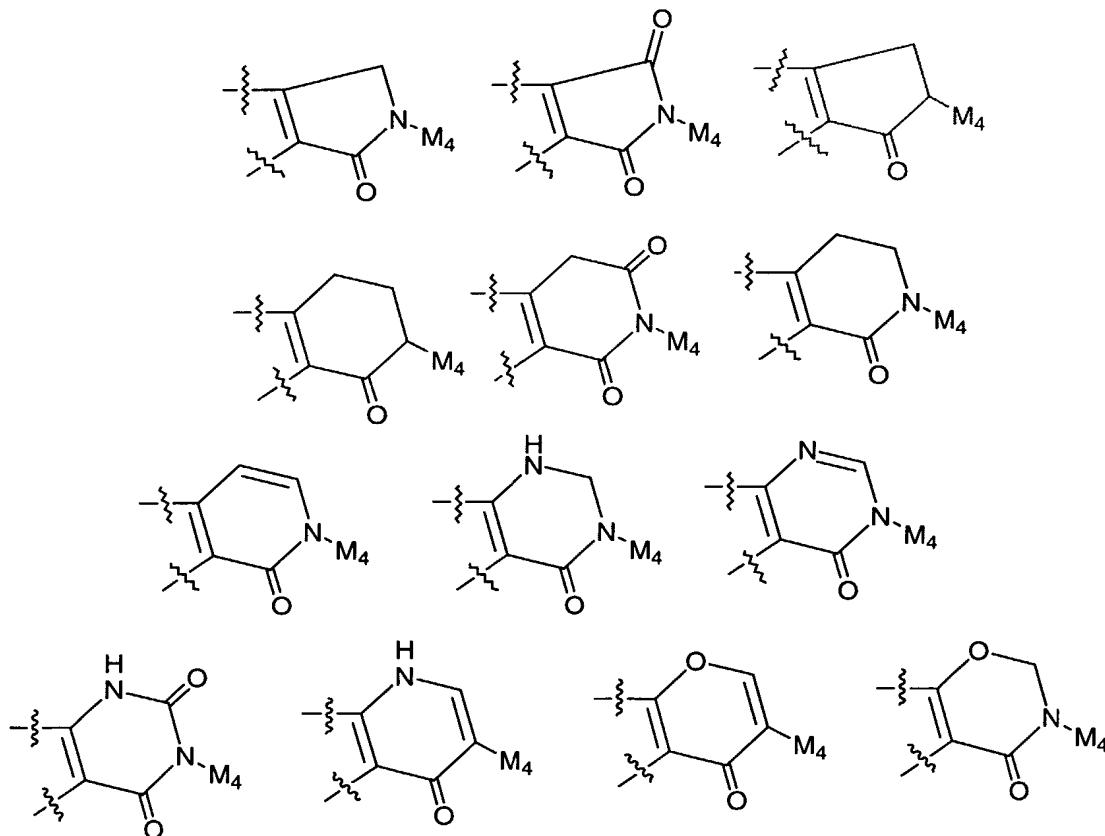
5 R⁶, at each occurrence, is selected from H, OH, OR², F, Cl, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, -CN, NO₂, NR²R^{2a}, CH₂NR²R^{2a}, C(O)R^{2b}, CH₂C(O)R^{2b}, NR²C(O)R^{2b}, and SO₂NR²R^{2a}; and,

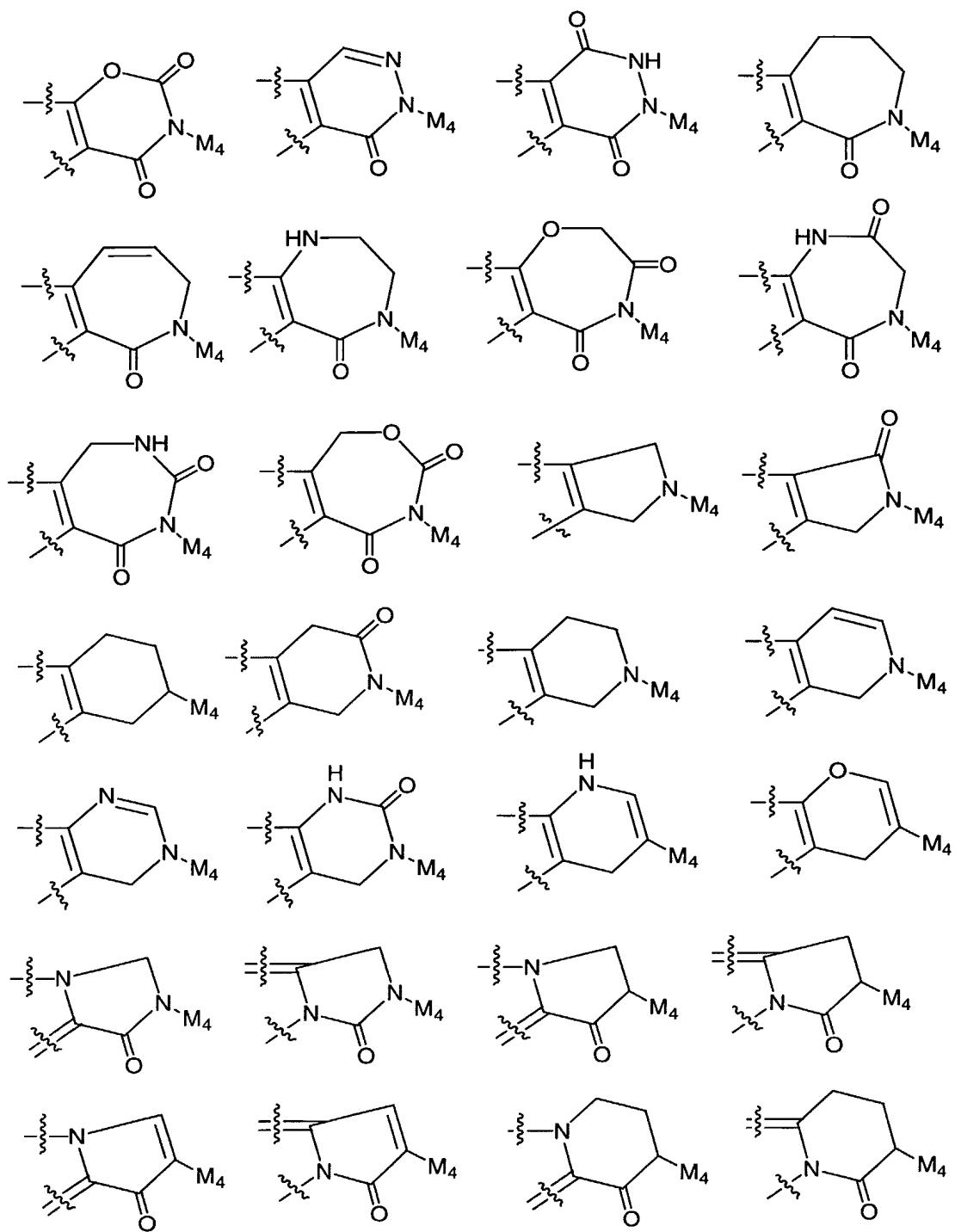
r, at each occurrence, is selected from 0, 1, and 2.

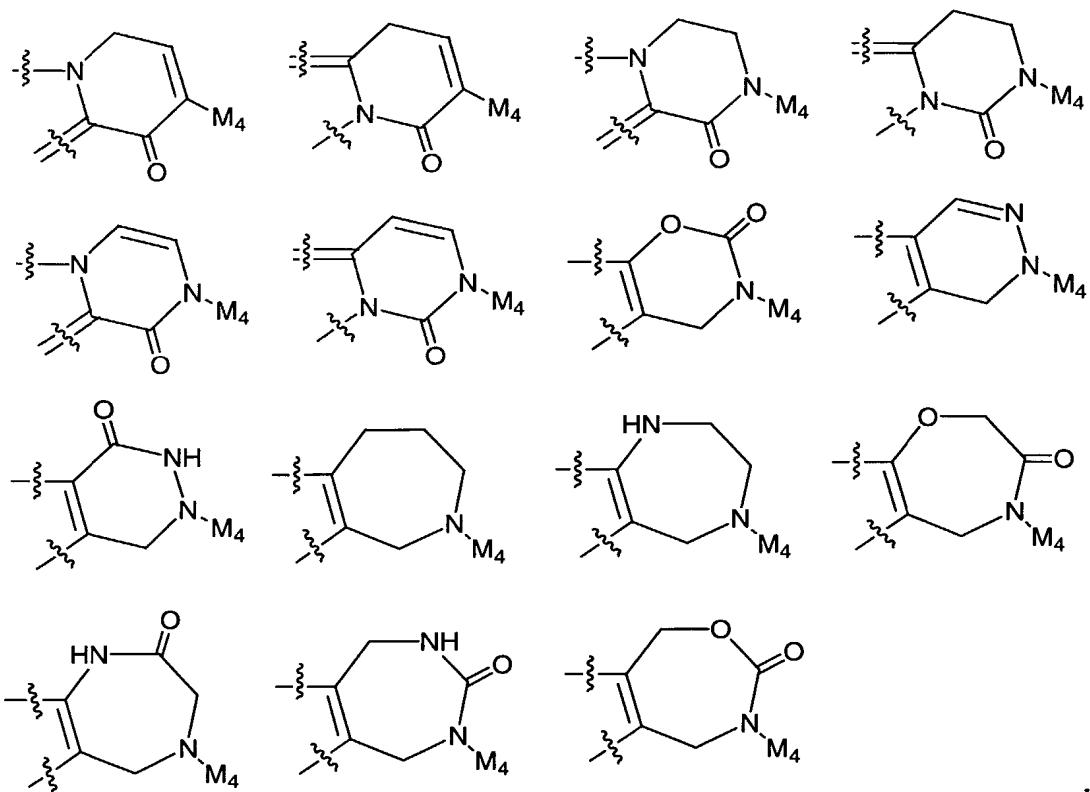
10

[5] In another preferred embodiment, the present invention provides a novel compound, wherein:

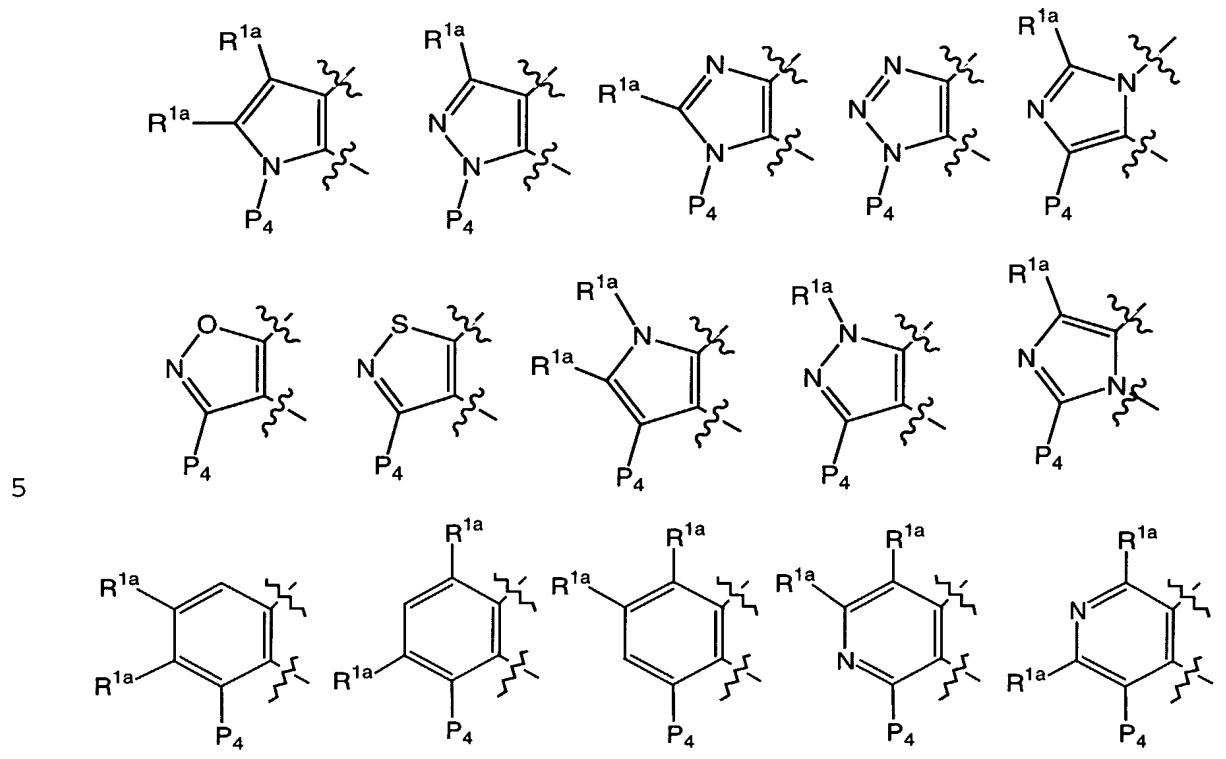
15 ring M is substituted with 0-1 R^{1a} and is selected from the group:





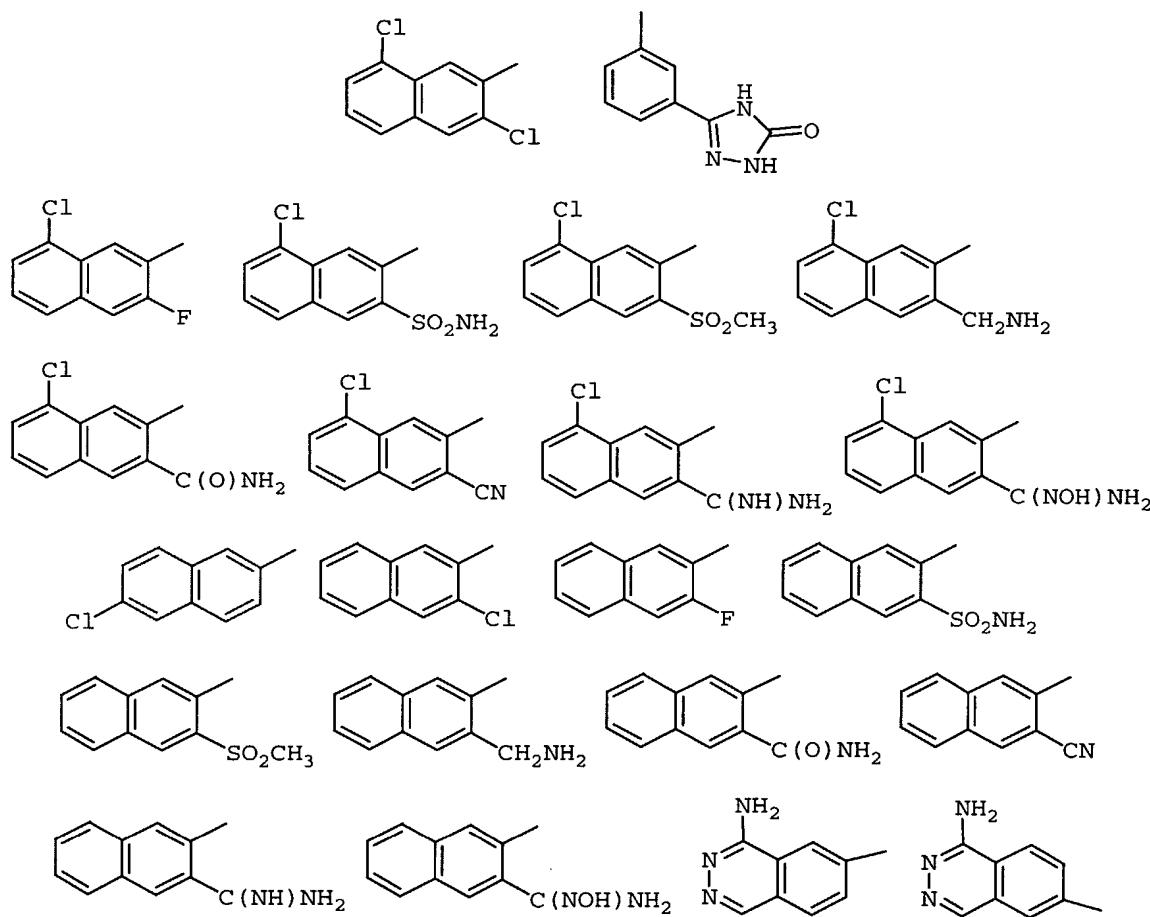


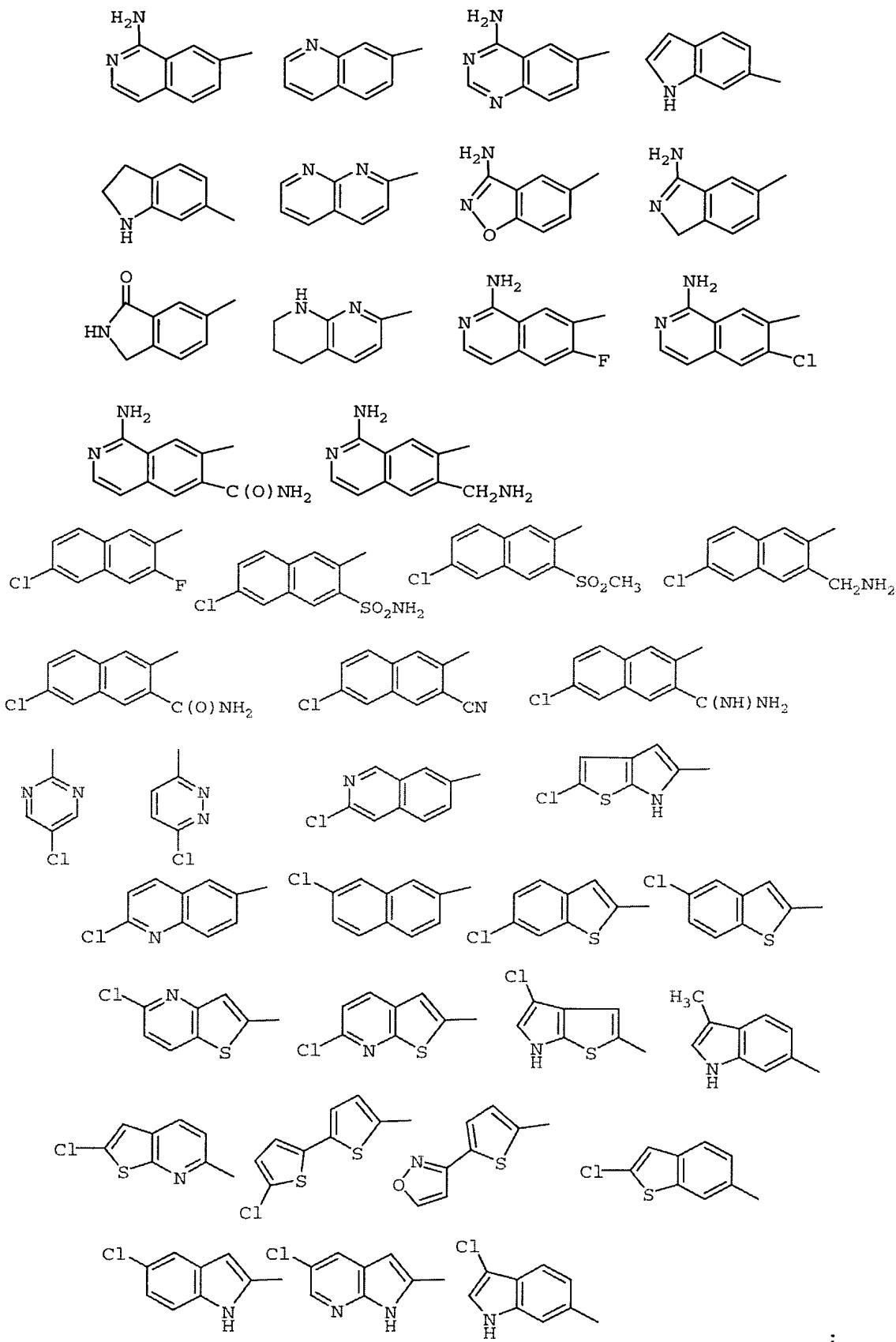
ring P, including P₁, P₂, P₃, and P₄ is selected from group:



-G is selected from:

2-amido-4-methoxy-phenyl; 2-amido-phenyl;
 2-aminomethyl-3-fluoro-phenyl;
 2-aminomethyl-4-fluoro-phenyl;
 5 2-aminomethyl-5-fluoro-phenyl;
 2-aminomethyl-6-fluoro-phenyl; 2-aminomethyl-phenyl;
 2-amino-pyrid-4-yl; 2-aminosulfonyl-4-methoxy-phenyl;
 2-aminosulfonyl-phenyl; 3-amido-phenyl;
 3-amino-4-chloro-phenyl; 3-aminomethyl-phenyl;
 10 3-chloro-phenyl; 4-chloro-phenyl; 4-ethyl-phenyl;
 4-methoxy-phenyl; 5-chloro-pyrid-2-yl; 5-chloro-thien-2-yl;
 6-amino-5-chloro-pyrid-2-yl; 6-amino-pyrid-2-yl;





A is selected from the group: cyclohexyl, piperidinyl, phenyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl;

5

Y is selected from $C(CH_3)_2$, $C(CH_2CH_3)_2$, cyclopropyl, cyclobutyl, cyclopentyl, 2-cyclopentanonyl, cyclohexyl, 2-cyclohexanonyl, pyrrolidinyl (attached to A and R^{4a} at the 2-position), pyrrolidinyl (attached to A and R^{4a} at the 3-position), 2-pyrrolidinonyl (attached to A and R^{4a} at the 3-position), piperidinyl (attached to A and R^{4a} at the 4-position), 4-piperdinonyl (attached to A and R^{4a} at the 3-position), tetrahydrofuranyl, and tetrahydropyranyl (attached to A and R^{4a} at the 4-position);

R^{1a} , at each occurrence, is selected from H, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, CH_2F , CH_2Cl , Br, CH_2Br , -CN, CH_2CN , CF_3 , CH_2CF_3 , OCH_3 , CH_2OH , $C(CH_3)_2OH$, CH_2OCH_3 , NH_2 , CH_2NH_2 , $NHCH_3$, CH_2NHCH_3 , $N(CH_3)_2$, $CH_2N(CH_3)_2$, CO_2H , $COCH_3$, CO_2CH_3 , $CH_2CO_2CH_3$, SCH_3 , CH_2SCH_3 , $S(O)CH_3$, $CH_2S(O)CH_3$, $S(O)_2CH_3$, $CH_2S(O)_2CH_3$, $C(O)NH_2$, $CH_2C(O)NH_2$, SO_2NH_2 , $CH_2SO_2NH_2$, $NHSO_2CH_3$, $CH_2NHSO_2CH_3$, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridin-2-yl-N-oxide, pyridin-3-yl-N-oxide, pyridin-4-yl-N-oxide, imidazol-1-yl, CH_2 -imidazol-1-yl, 4-methyl-oxazol-2-yl, 4-N,N-dimethylaminomethyl-oxazol-2-yl, 1,2,3,4-tetrazol-1-yl, 1,2,3,4-tetrazol-5-yl, CH_2 -1,2,3,4-tetrazol-1-yl, and CH_2 -1,2,3,4-tetrazol-5-yl, provided that R^{1a} forms other than an N-halo, N-S, or N-CN bond;

R^2 , at each occurrence, is selected from H, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, phenyl substituted with 0-1 R^{4b} , benzyl substituted with 0-1 R^{4b} , and 5 membered

aromatic heterocycle substituted with 0-1 R^{4b} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p;

5 R^{2a}, at each occurrence, is selected from H, CH₃, and CH₂CH₃;

10 alternatively, R² and R^{2a}, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-1 R^{4b} and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)_p;

15 R^{2b}, at each occurrence, is selected from OH, OCH₃, OCH₂CH₃, CH₃, and CH₂CH₃;

R^{2c}, at each occurrence, is selected from OH, OCH₃, OCH₂CH₃, CH₃, and CH₂CH₃;

20 R^{2d}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, C₃₋₆ cycloalkyl substituted with 0-2 R^{4c}, phenyl substituted with 0-2 R^{4c}, and 5-6 membered aromatic heterocycle substituted with 0-2 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2d} forms other than a N-halo, N-C-halo, S(O)_p-halo, O-halo, N-S, S-N, S(O)_p-S(O)_p, S-O, O-N, O-S, or O-O moiety;

30 R^{2e}, at each occurrence, is selected from H, R^{4c}, C₁₋₄ alkyl substituted with 0-2 R^{4c}, C₃₋₆ cycloalkyl substituted with 0-2 R^{4c}, phenyl substituted with 0-2 R^{4c}, and 5-6 membered aromatic heterocycle substituted with 0-2 R^{4c}

and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2e} forms other than a C(O)-halo or C(O)-S(O)_p moiety;

5

R^{4a} is selected from -(CH₂)_r-5-6 membered carbocycle substituted with 0-3 R^{4c}, -(CH₂)_r-5-6 membered heterocycle substituted with 0-3 R^{4c} and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, (CH₂)_rNR^{2d}R^{2d}, (CH₂)_rN(→O)R^{2d}R^{2d}, (CH₂)_rOR^{2d}, (CH₂)_r-C(O)NR^{2d}R^{2d}, (CH₂)_r-NR^{2d}C(O)R^{2e}, (CH₂)_r-C(O)R^{2e}, (CH₂)_r-NR^{2d}C(O)NR^{2d}R^{2d}, (CH₂)_r-NR^{2d}C(O)OR^{2d}, (CH₂)_r-NR^{2d}SO₂R^{2d}, and (CH₂)_r-S(O)_pR^{2d}, provided that S(O)_pR^{2d} forms other than S(O)₂H or S(O)H;

10

15

20

R^{4b}, at each occurrence, is selected from H, =O, OR³, CH₂OR³, F, Cl, CH₃, CH₂CH₃, NR³R^{3a}, CH₂NR³R^{3a}, C(O)R³, C(O)OR^{3c}, NR³C(O)R^{3a}, C(O)NR³R^{3a}, SO₂NR³R^{3a}, NR³SO₂-phenyl, S(O)₂CH₃, S(O)₂-phenyl, and CF₃;

25

30

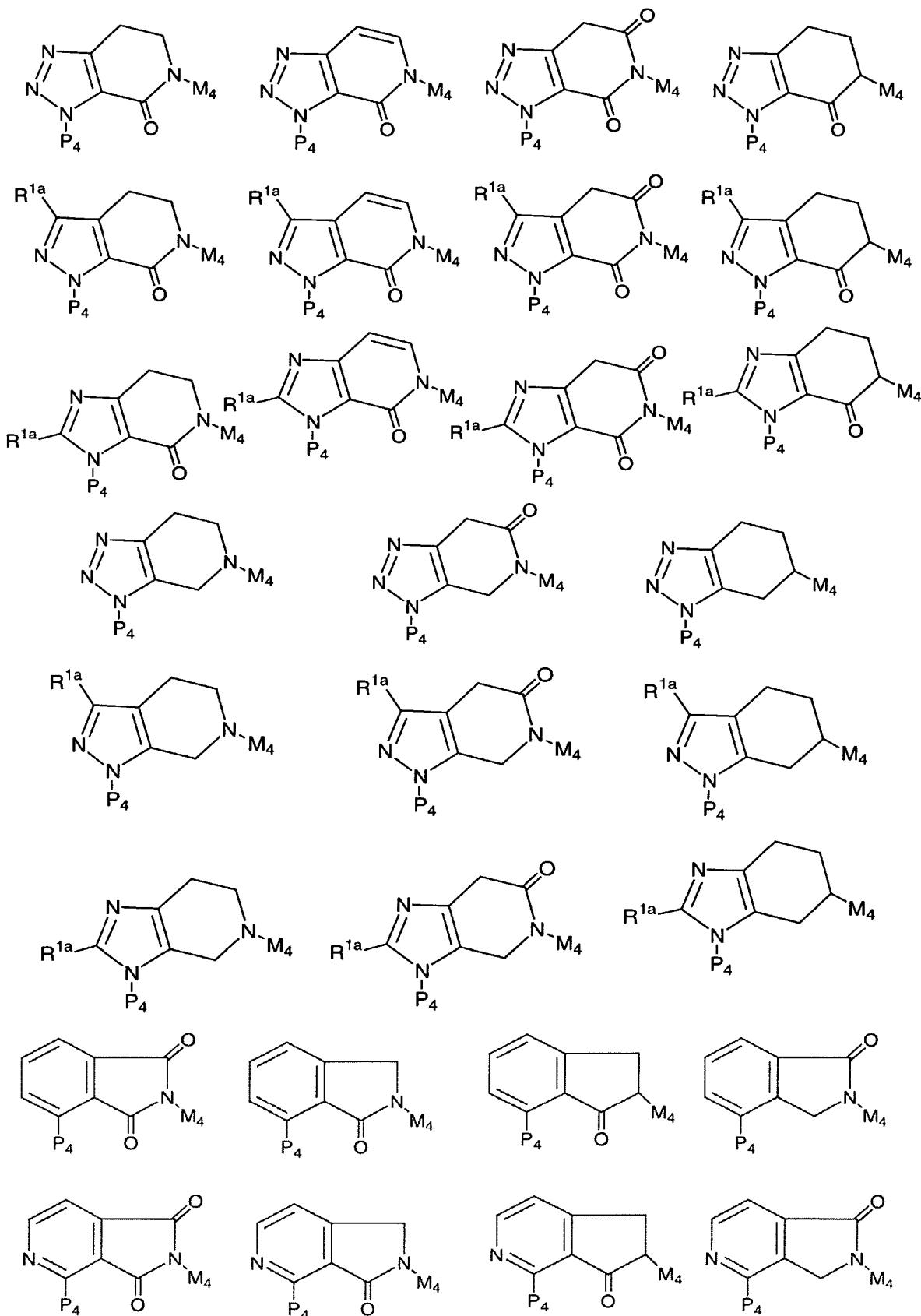
R^{4c}, at each occurrence, is selected from =O, OH, OCH₃, OCH₂CH₃, OCH₂CH₂CH₃, OCH(CH₃)₂, CH₃, CH₂CH₃, CH₂CH₂CH₃, CH(CH₃)₂, C₂₋₃ alkenyl, C₂₋₃ alkynyl, CH₂OH, CH₂OCH₃, CH₂OCH₂CH₃, CH₂OCH₂CH₂CH₃, CH₂OCH(CH₃)₂, F, Br, Cl, CF₃, NR²R^{2a}, CH₂NR²R^{2a}, N(→O)R²R^{2a}, CH₂N(→O)R²R^{2a}, C(O)R^{2c}, CH₂C(O)R^{2c}, NR²C(O)R^{2b}, CH₂NR²C(O)R^{2b}, C(O)NR²R^{2a}, CH₂C(O)NR²R^{2a}, SO₂NR²R^{2a}, CH₂SO₂NR²R^{2a}, NR²SO₂R^{5a}, CH₂NR²SO₂R^{5a}, S(O)_pR^{5a}, CH₂S(O)_pR^{5a}, CF₃, cyclopropyl substituted with 0-1 R^{4b}, cyclobutyl substituted with 0-1 R^{4b}, cyclopentyl substituted with 0-1 R^{4b}, phenyl substituted with 0-1 R^{4b}, -CH₂-cyclopropyl substituted

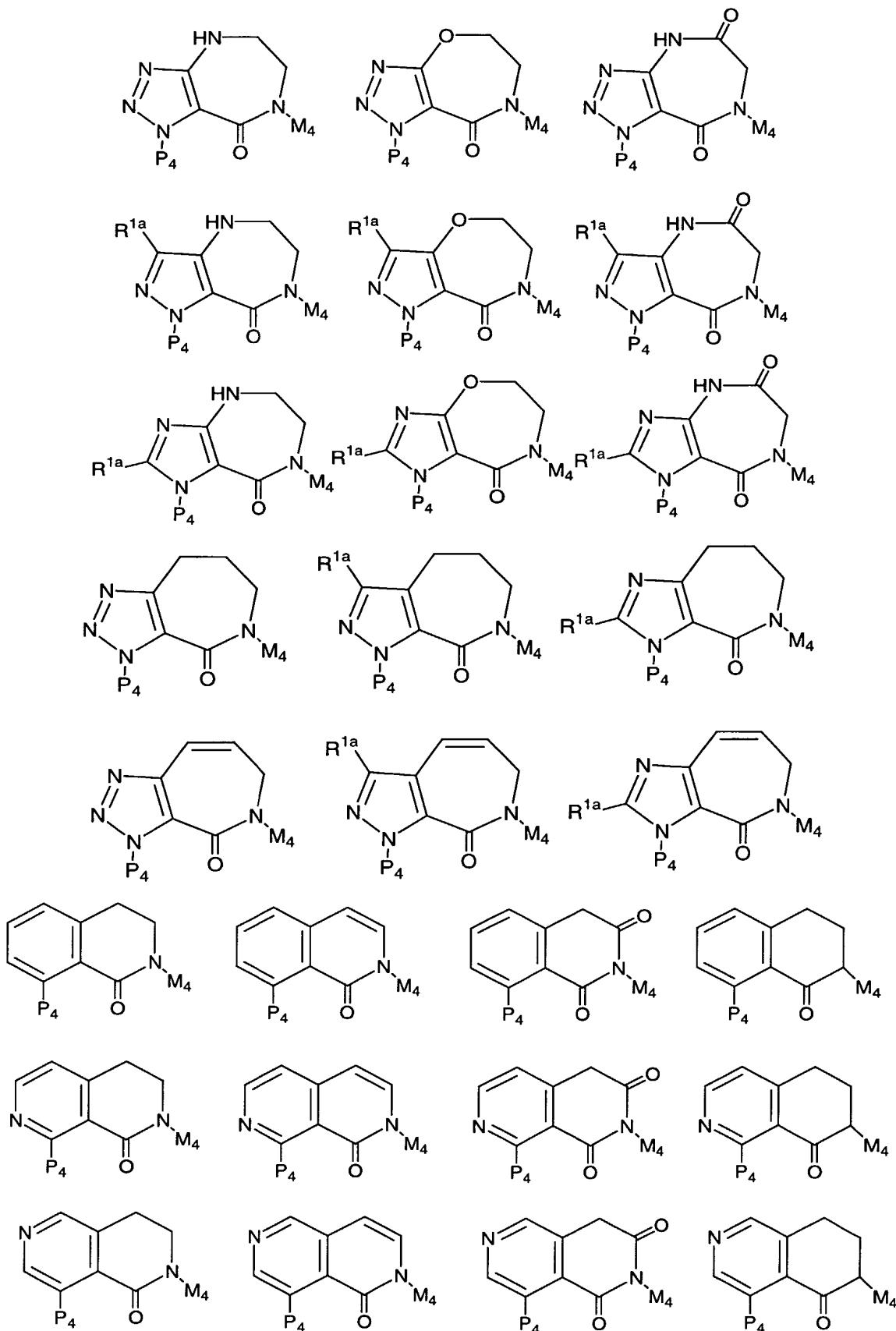
with 0-1 R^{4b}, -CH₂-cyclobutyl substituted with 0-1 R^{4b}, -CH₂-cyclopentyl substituted with 0-1 R^{4b}, benzyl substituted with 0-2 R^{4b}, 5-6 membered aromatic heterocycle substituted with 0-2 R^{4b} and consisting of 5 carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, and (CH₂)5-6 membered aromatic heterocycle substituted with 0-2 R^{4b} and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, 10 O, and S(O)_p;

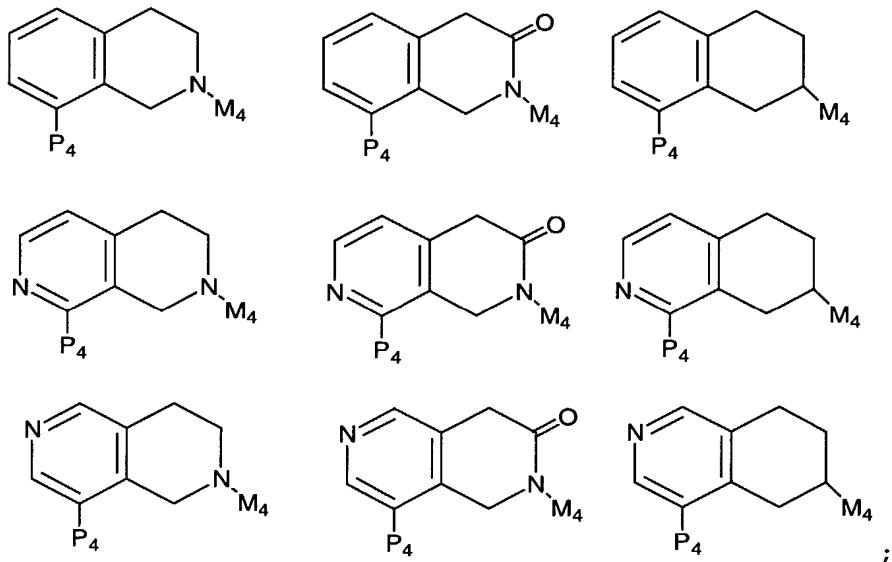
R⁵, at each occurrence, is selected from H, =O, CH₃, CH₂CH₃, OR³, CH₂OR³, F, Cl, NR³R^{3a}, CH₂NR³R^{3a}, C(O)R³, C(O)OR^{3c}, NR³C(O)R^{3a}, C(O)NR³R^{3a}, SO₂NR³R^{3a}, NR³SO₂-C₁₋₄ alkyl, 15 NR³SO₂-phenyl, S(O)₂-CH₃, S(O)₂-phenyl, CF₃, phenyl substituted with 0-2 R⁶, naphthyl substituted with 0-2 R⁶, and benzyl substituted with 0-2 R⁶; and,

R⁶, at each occurrence, is selected from H, OH, OR², F, Cl, 20 CH₃, CH₂CH₃, NR²R^{2a}, CH₂NR²R^{2a}, C(O)R^{2b}, CH₂C(O)R^{2b}, NR²C(O)R^{2b}, and SO₂NR²R^{2a}.

[6] In another preferred embodiment, the present invention 25 provides a novel compound, wherein the compound is selected from:





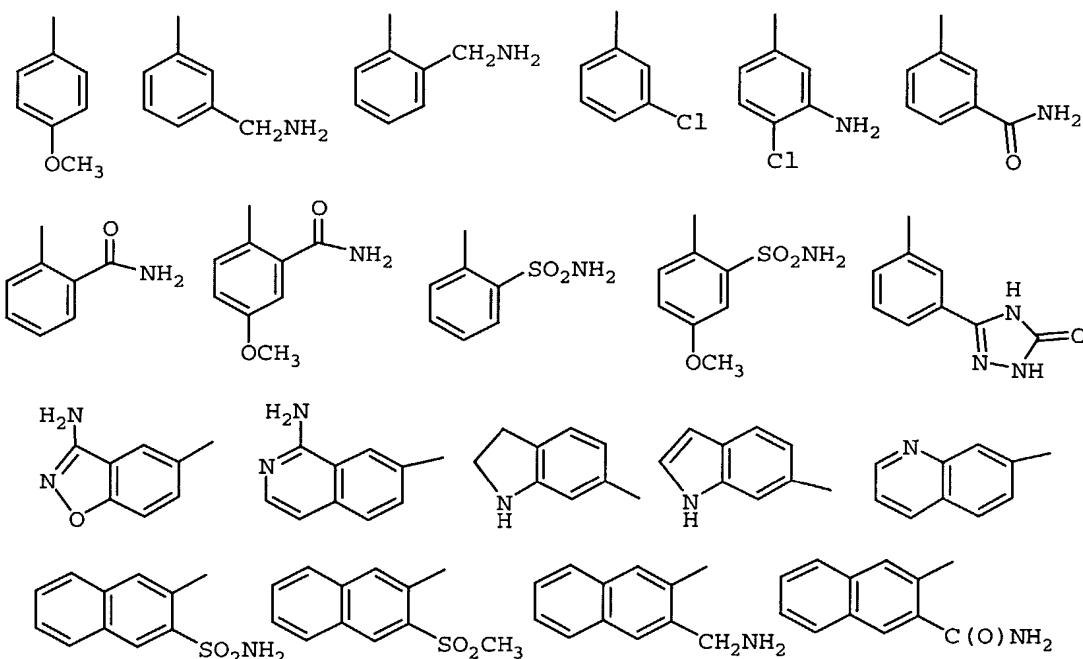


P₄ is -G₁-G;

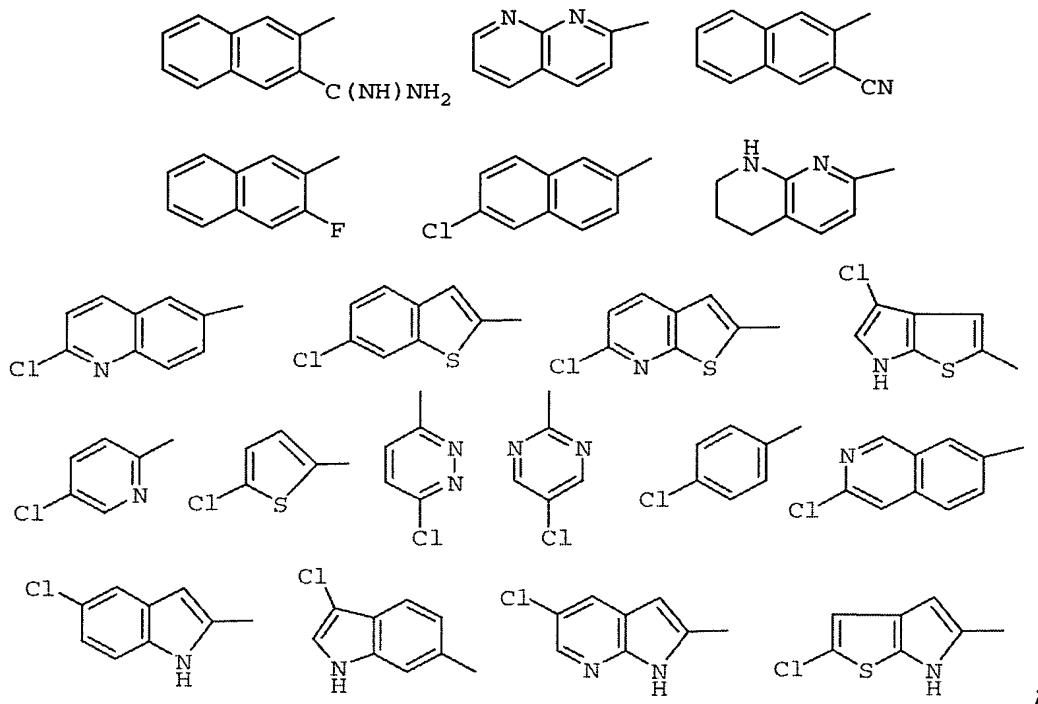
5

M₄ is -A-B;

-G is selected from:



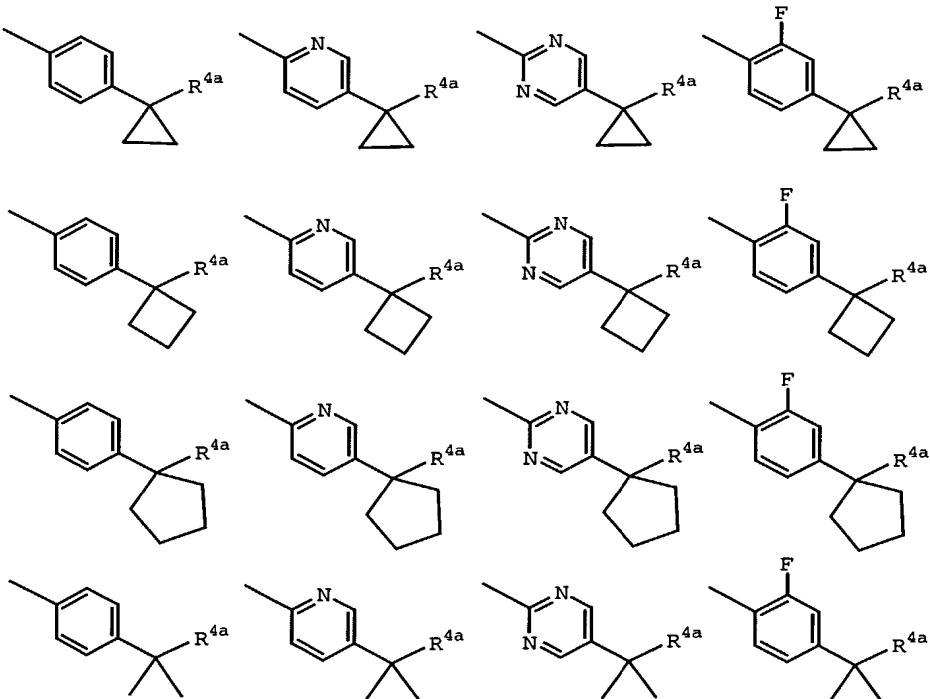
10

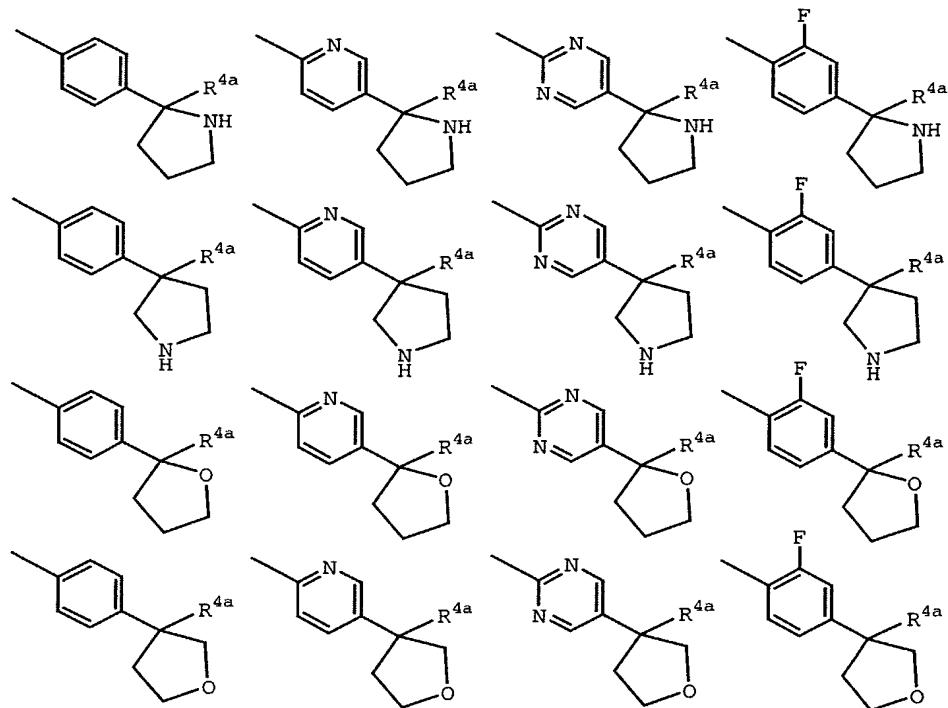


G_1 is absent or is selected from $C(O)NH$, $NHC(O)$, and $NHSO_2$;

5

$A-B$ is selected from:





Z is selected from a bond, CH₂, and CH₂CH₂;

5 R^{2d}, at each occurrence, is selected from H, C₁₋₄ alkyl substituted with 0-1 R^{4c}, C₃₋₆ cycloalkyl substituted with 0-2 R^{4c}, phenyl substituted with 0-2 R^{4c}, and a 5-6 membered aromatic heterocycle consisting of:
 10 carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2d} forms other than a N-halo, N-C-halo, S(O)_p-halo, O-halo, N-S, S-N, S(O)_p-S(O)_p, S-O, O-N, O-S, or O-O moiety;

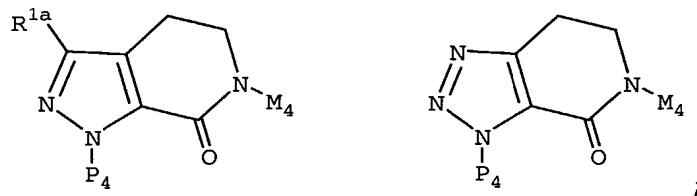
15 R^{2e}, at each occurrence, is selected from H, C₁₋₄ alkyl substituted with 0-1 R^{4c}, C₃₋₆ cycloalkyl substituted with 0-2 R^{4c}, phenyl, substituted with 0-2 R^{4c}, and 5-6 membered aromatic heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)_p, provided that R^{2e} forms other than a C(O)-halo or C(O)-S(O)_p moiety;

R^{4a} is selected from $NR^{2d}R^{2d}$, $CH_2NR^{2d}R^{2d}$, $CH_2CH_2NR^{2d}R^{2d}$,
 $N(\rightarrow O)R^{2d}R^{2d}$, $CH_2N(\rightarrow O)R^{2d}R^{2d}$, CH_2OR^{2d} , $C(O)R^{2e}$,
 $C(O)NR^{2d}R^{2d}$, $CH_2C(O)NR^{2d}R^{2d}$, $NR^{2d}C(O)R^{2e}$, $CH_2NR^{2d}C(O)R^{2e}$,
5 $NR^{2d}C(O)NR^{2d}R^{2d}$, $CH_2NR^{2d}C(O)NR^{2d}R^{2d}$, $NR^{2d}C(O)OR^{2d}$,
 $CH_2NR^{2d}C(O)OR^{2d}$, $NR^{2d}SO_2R^{2d}$, $CH_2NR^{2d}SO_2R^{2d}$, $S(O)_pR^{2d}$,
 $CH_2S(O)_pR^{2d}$, 5-6 membered carbocycle substituted with
0-2 R^{4c} , $-(CH_2)-5-6$ membered carbocycle substituted
with 0-2 R^{4c} , $-(CH_2)_2-5-6$ membered carbocycle
10 substituted with 0-2 R^{4c} , 5-6 membered heterocycle
substituted with 0-2 R^{4c} and consisting of: carbon
atoms and 1-4 heteroatoms selected from the group
consisting of N, O, and $S(O)_p$, $-(CH_2)-5-6$ membered
heterocycle substituted with 0-2 R^{4c} and consisting of:
15 carbon atoms and 1-4 heteroatoms selected from the
group consisting of N, O, and $S(O)_p$, and $-(CH_2)_2-5-6$
membered heterocycle substituted with 0-2 R^{4c} and
consisting of: carbon atoms and 1-4 heteroatoms
selected from the group consisting of N, O, and $S(O)_p$
20 provided that $S(O)_pR^{2d}$ forms other than $S(O)_2H$ or
 $S(O)H$; and,

R^{4c} is selected from =O, OH, OCH_3 , OCH_2CH_3 , $OCH_2CH_2CH_3$,
 $OCH(CH_3)_2$, CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH=CH_2$,
25 $CH\equiv CH$, CH_2OH , CH_2OCH_3 , $CH_2OCH_2CH_3$, $CH_2OCH_2CH_2CH_3$,
 $CH_2OCH(CH_3)_2$, F, Br, Cl, CF_3 , NR^2R^{2a} , $CH_2NR^{2d}R^{2a}$,
 $C(O)R^{2c}$, $CH_2C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $CH_2NR^2C(O)R^{2b}$,
 $C(O)NR^2R^{2a}$, $CH_2C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $CH_2SO_2NR^2R^{2a}$,
 $NR^2SO_2R^{5a}$, $CH_2NR^2SO_2R^{5a}$, $S(O)_pR^{5a}$, and $CH_2S(O)_pR^{5a}$.

30

[7] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is selected from:

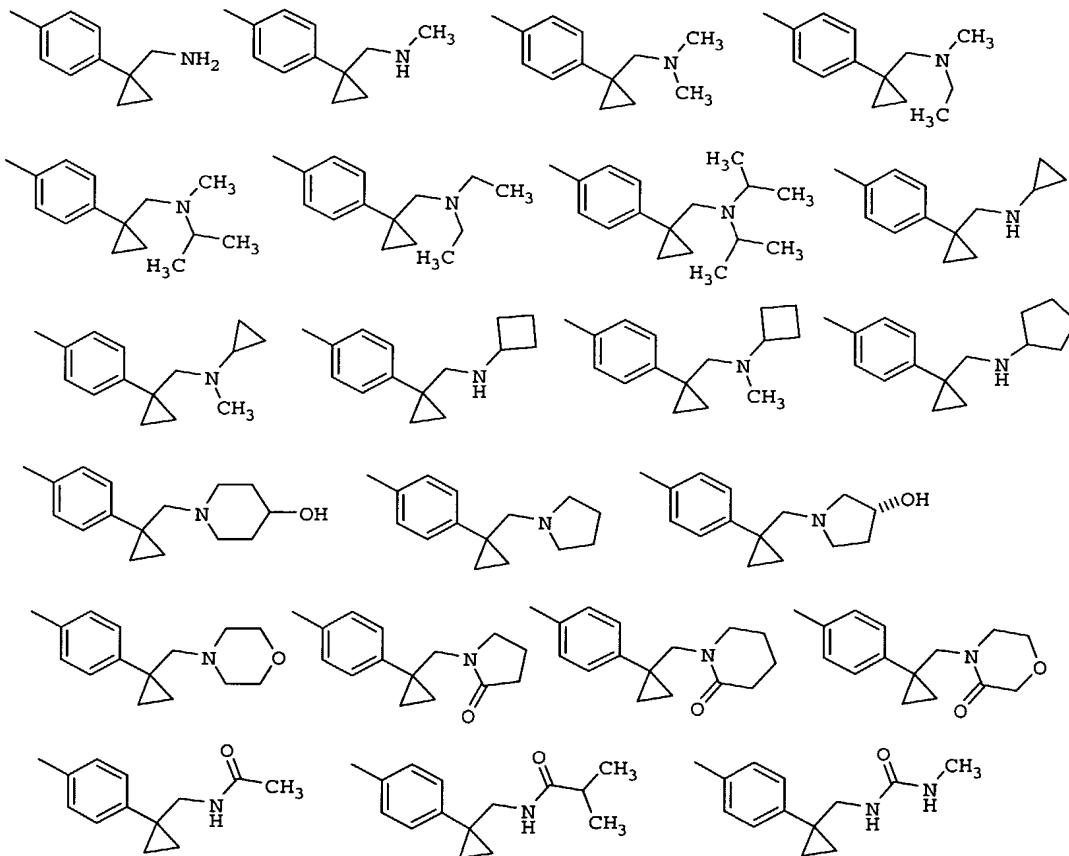


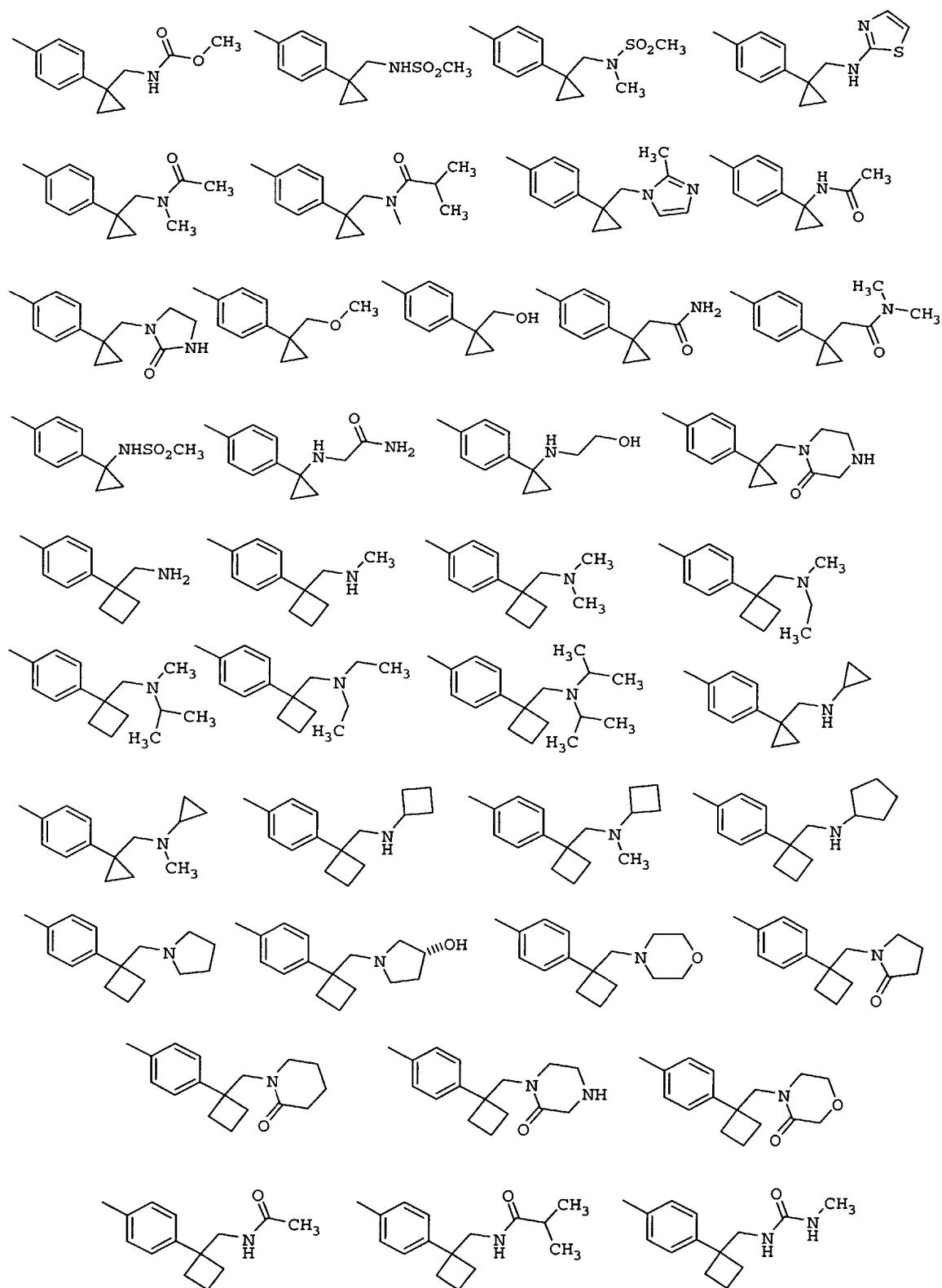
5 P₄ is -G;

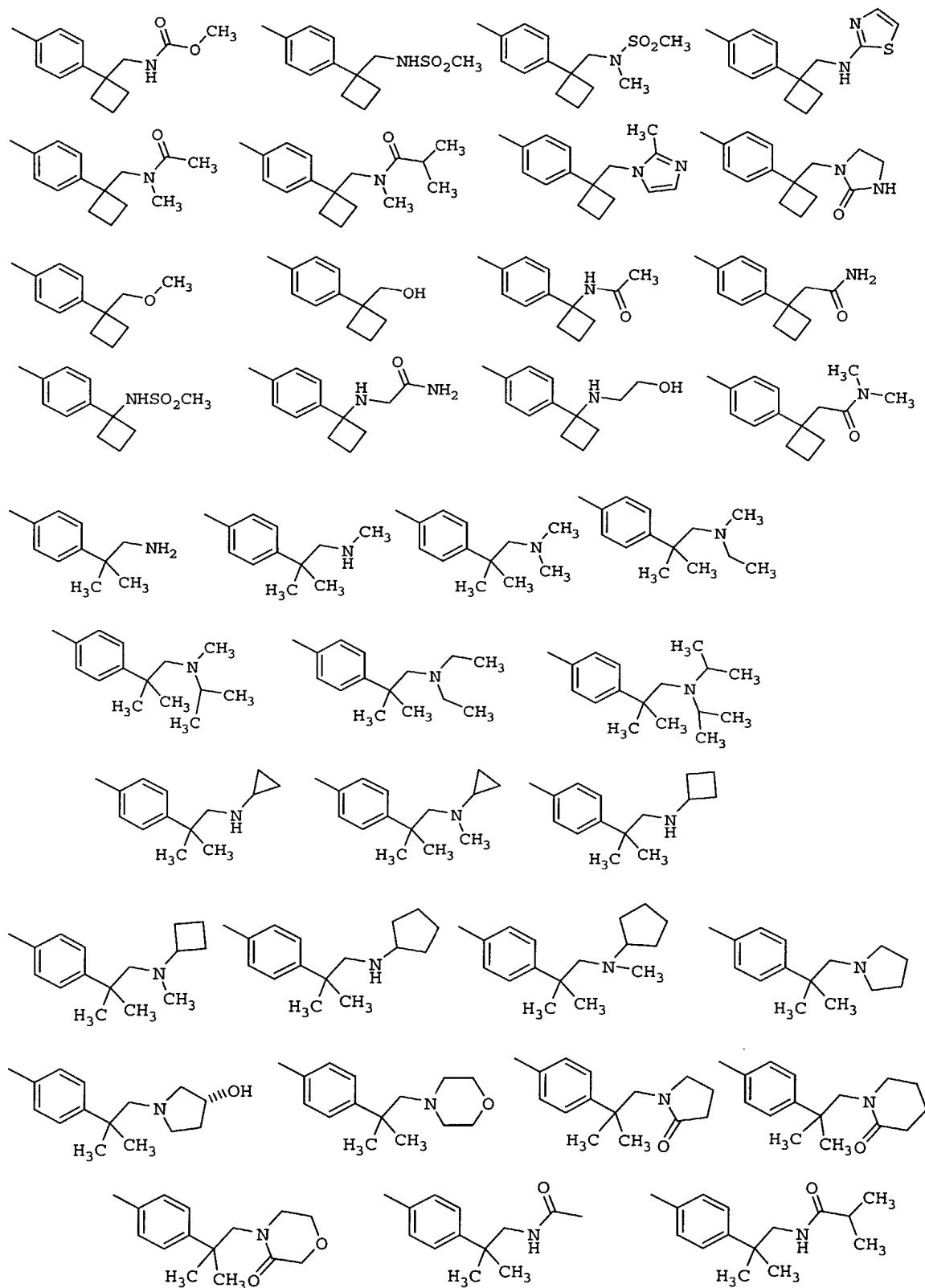
M₄ is -A-B;

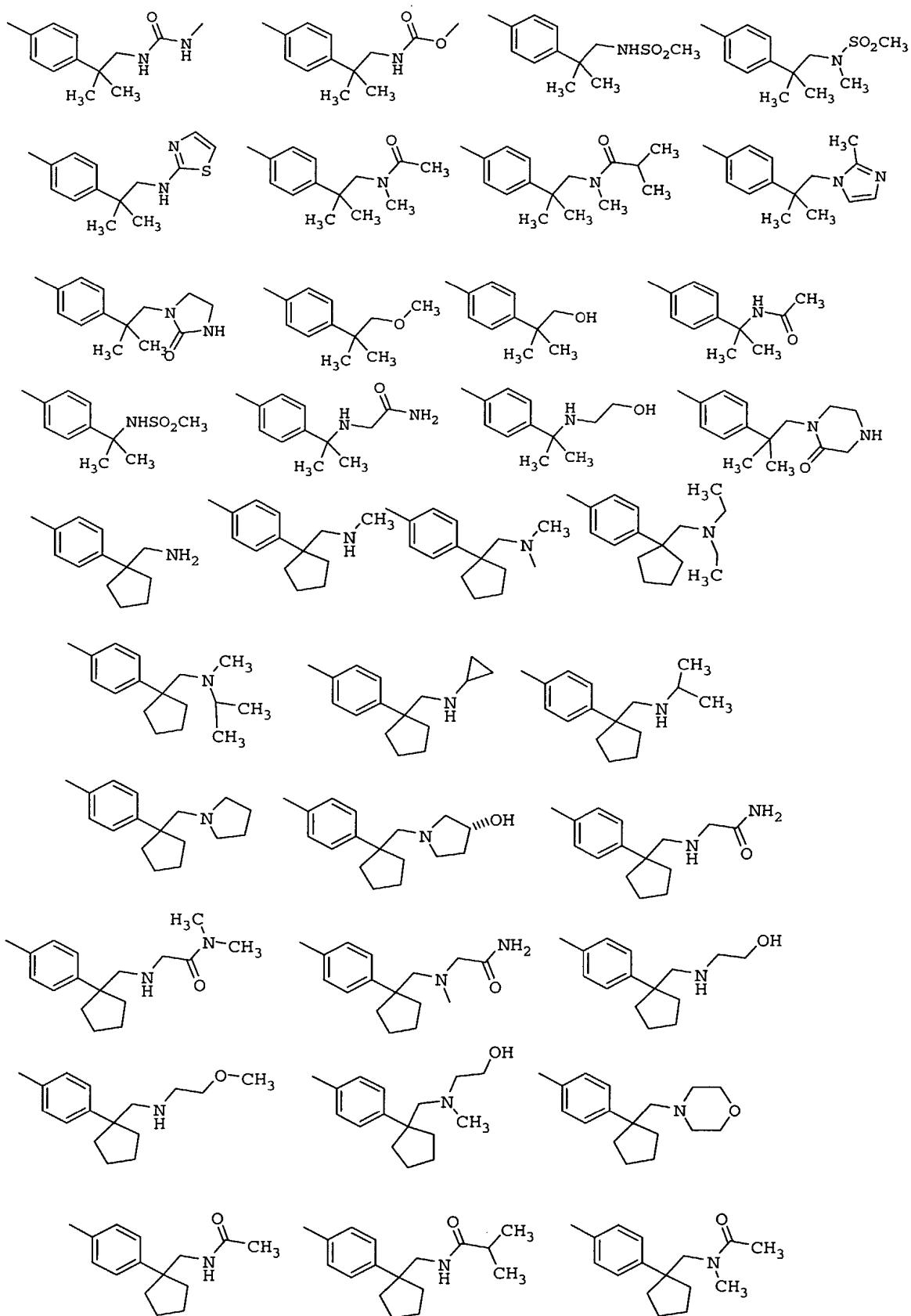
A-B is selected from:

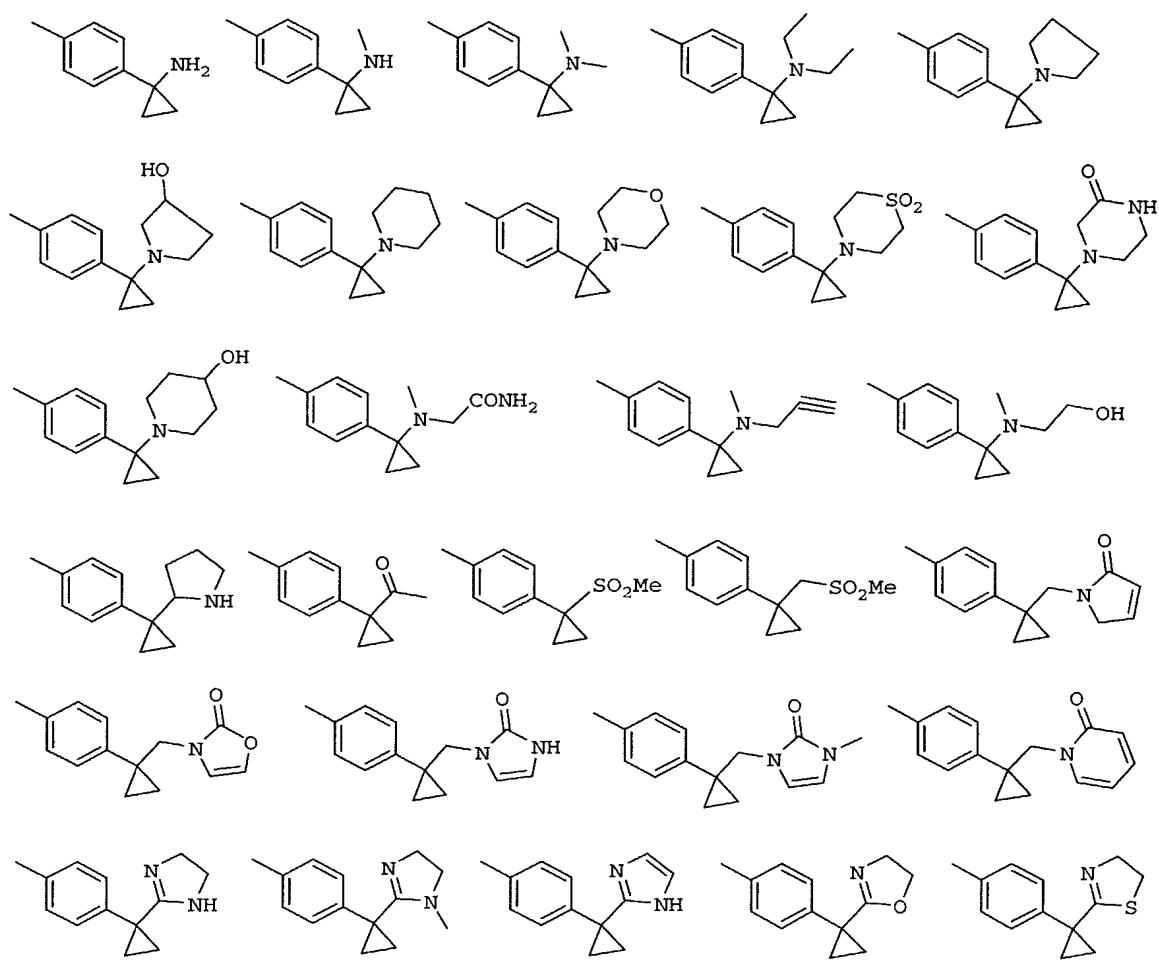
10

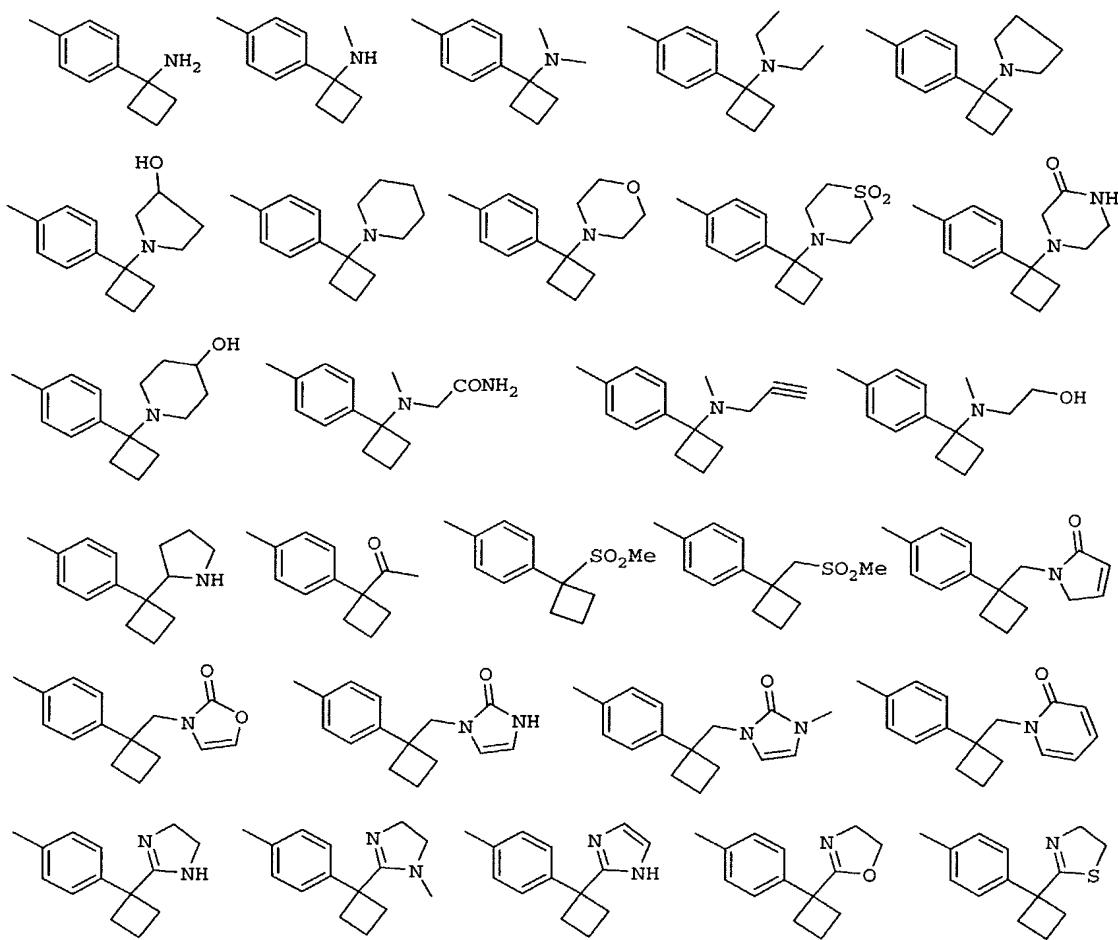


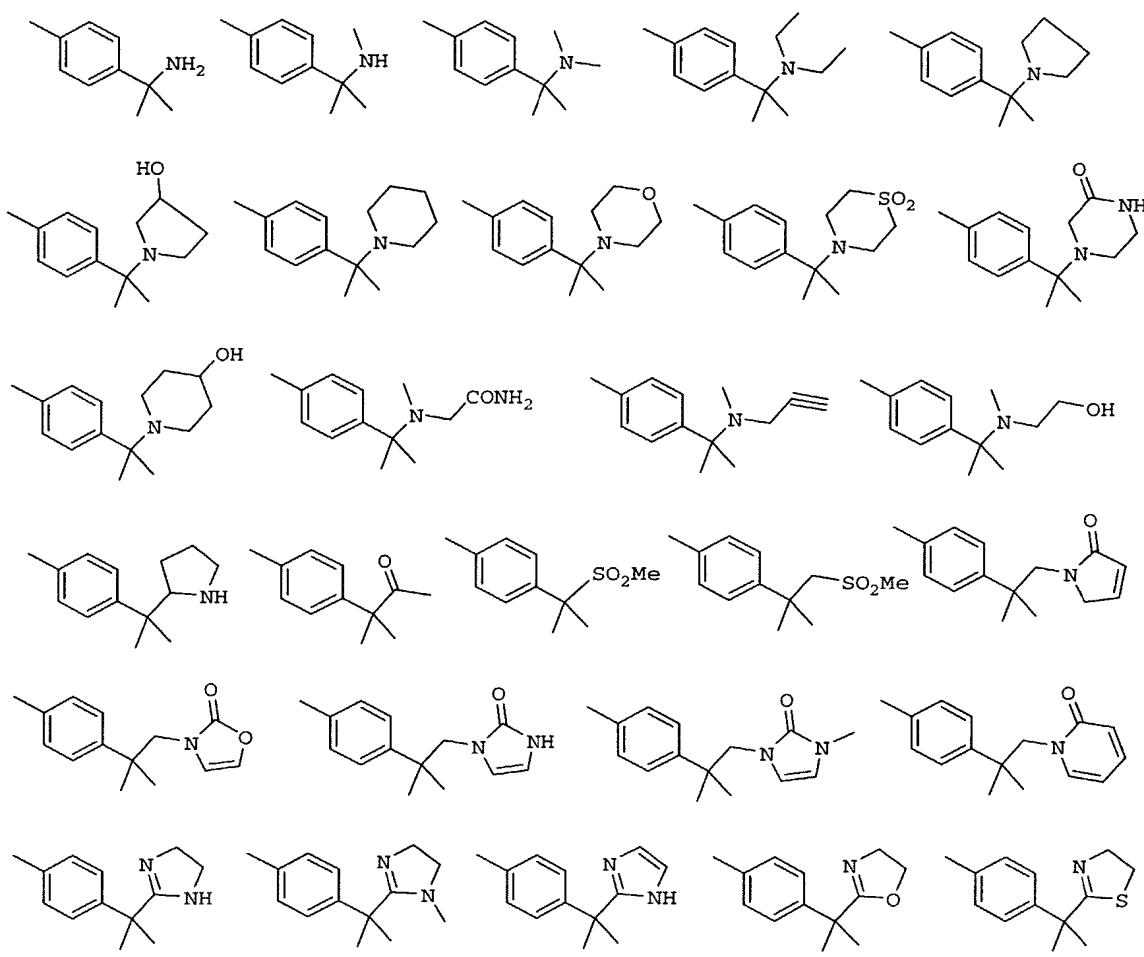


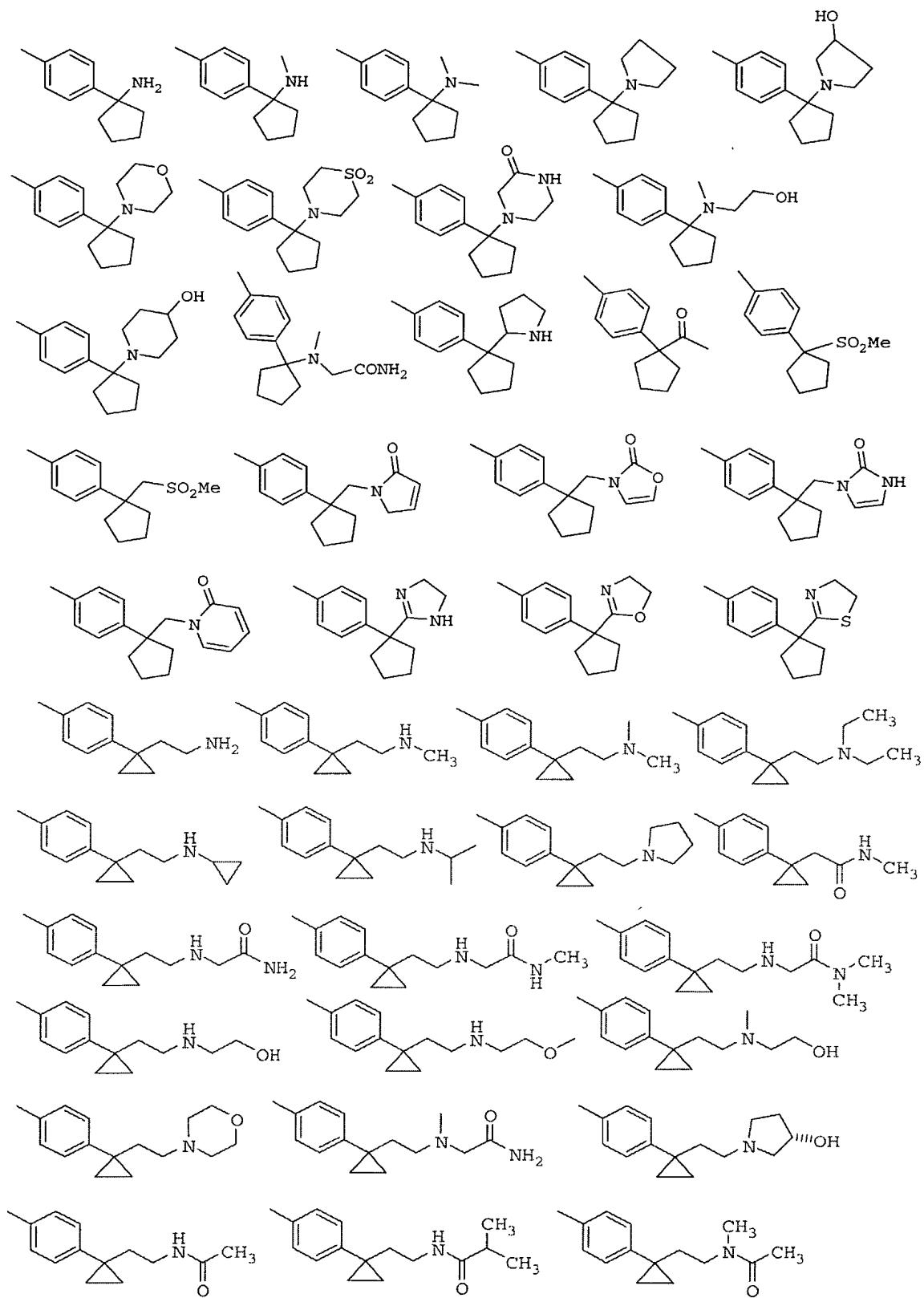


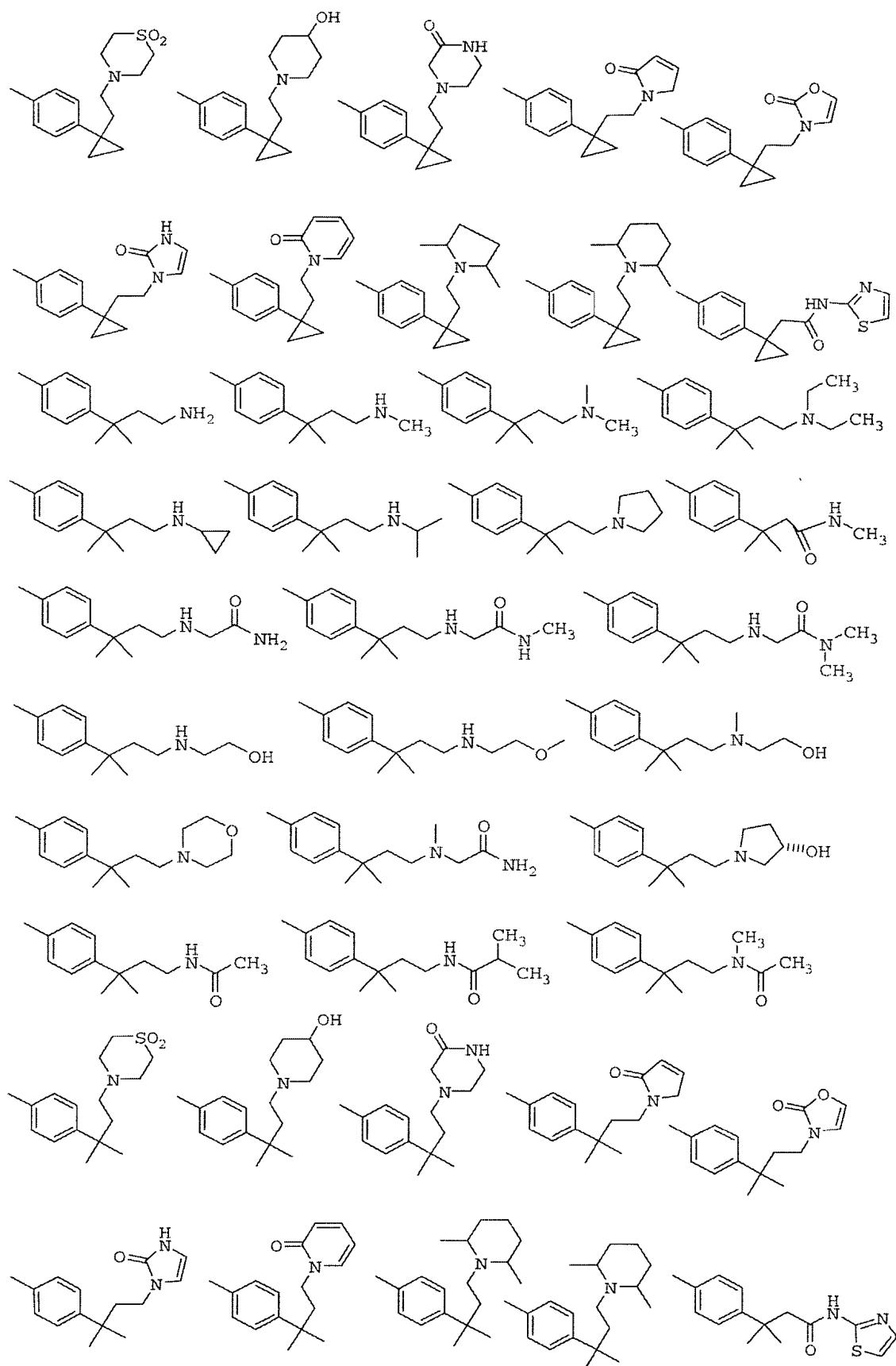


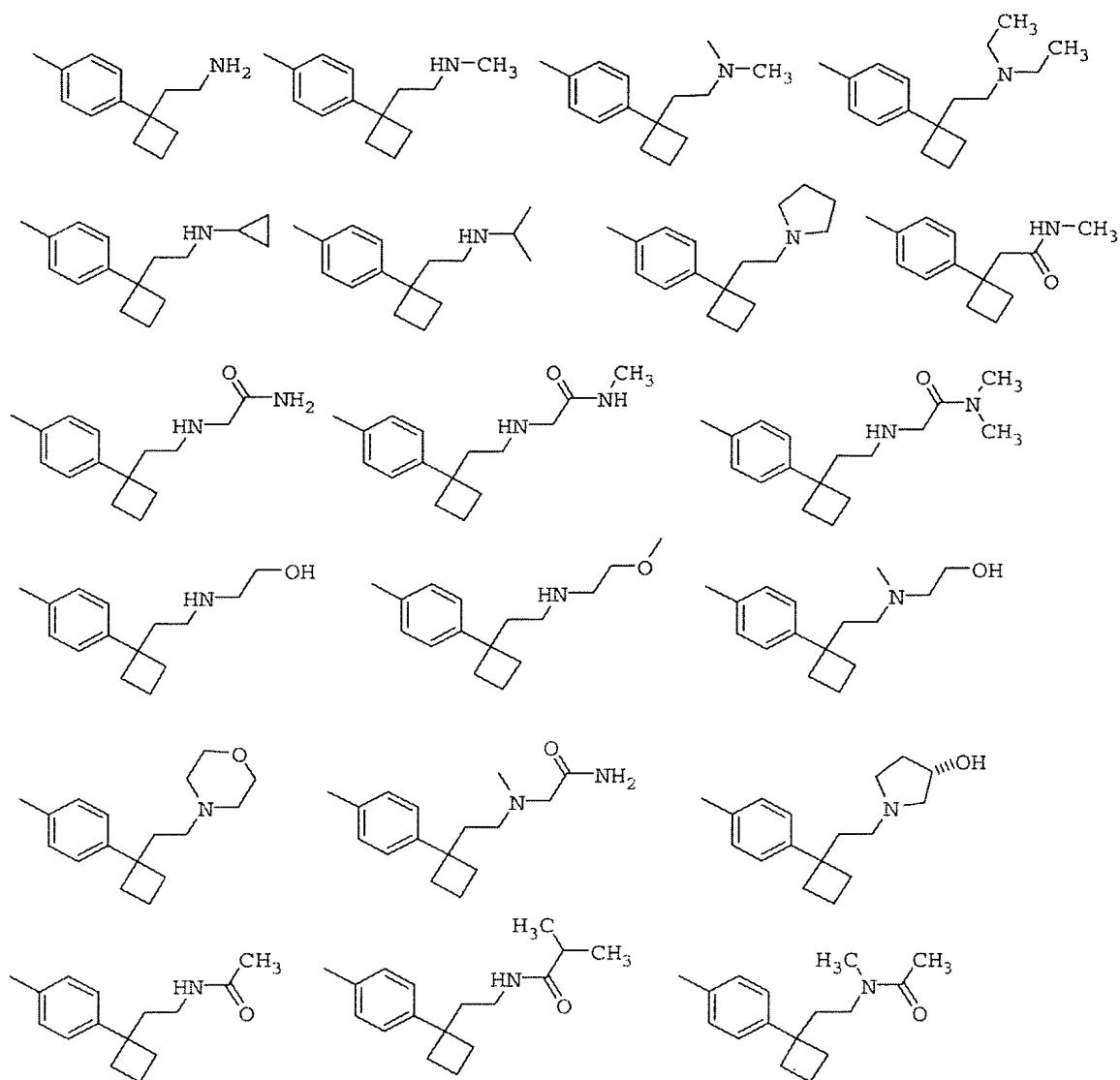


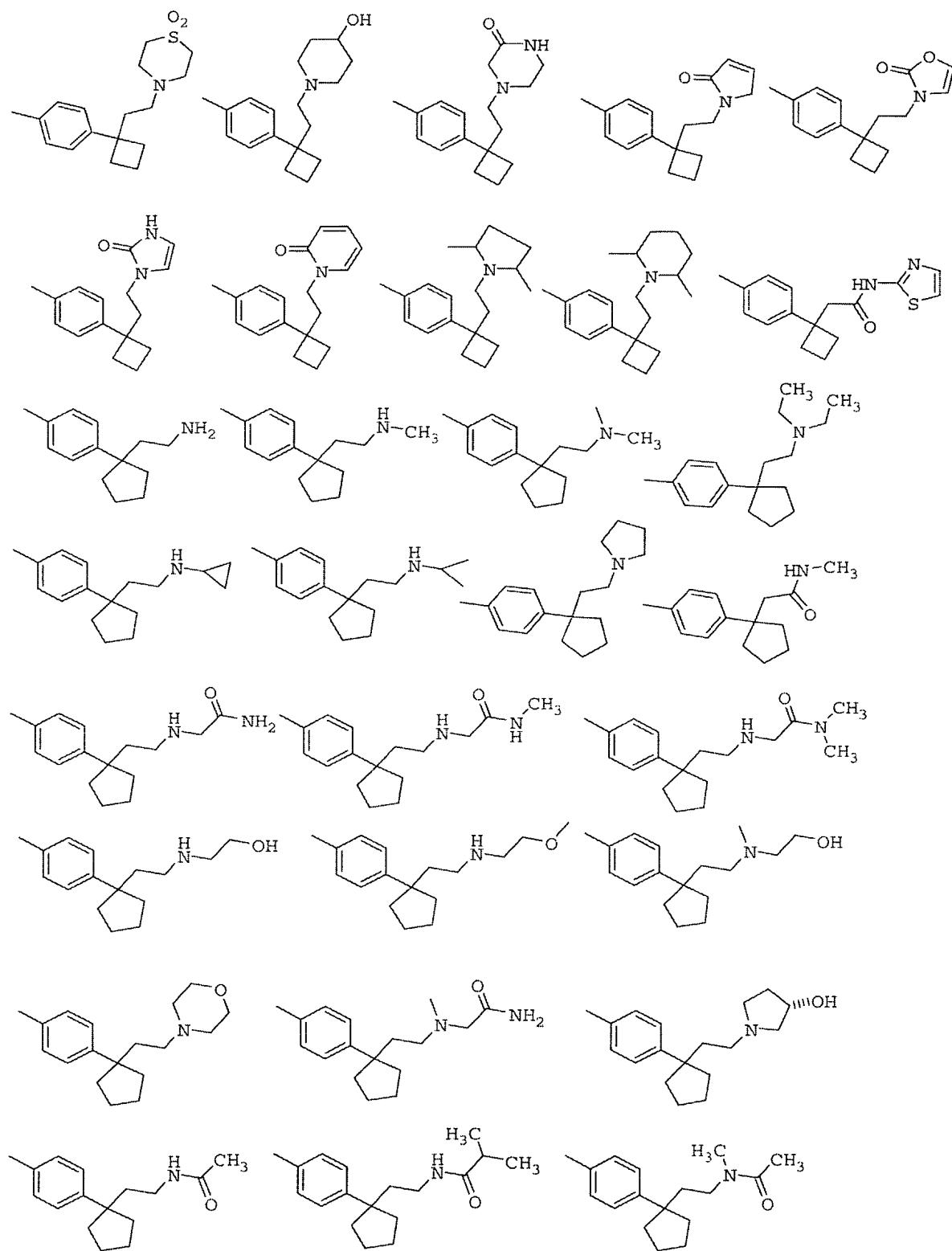


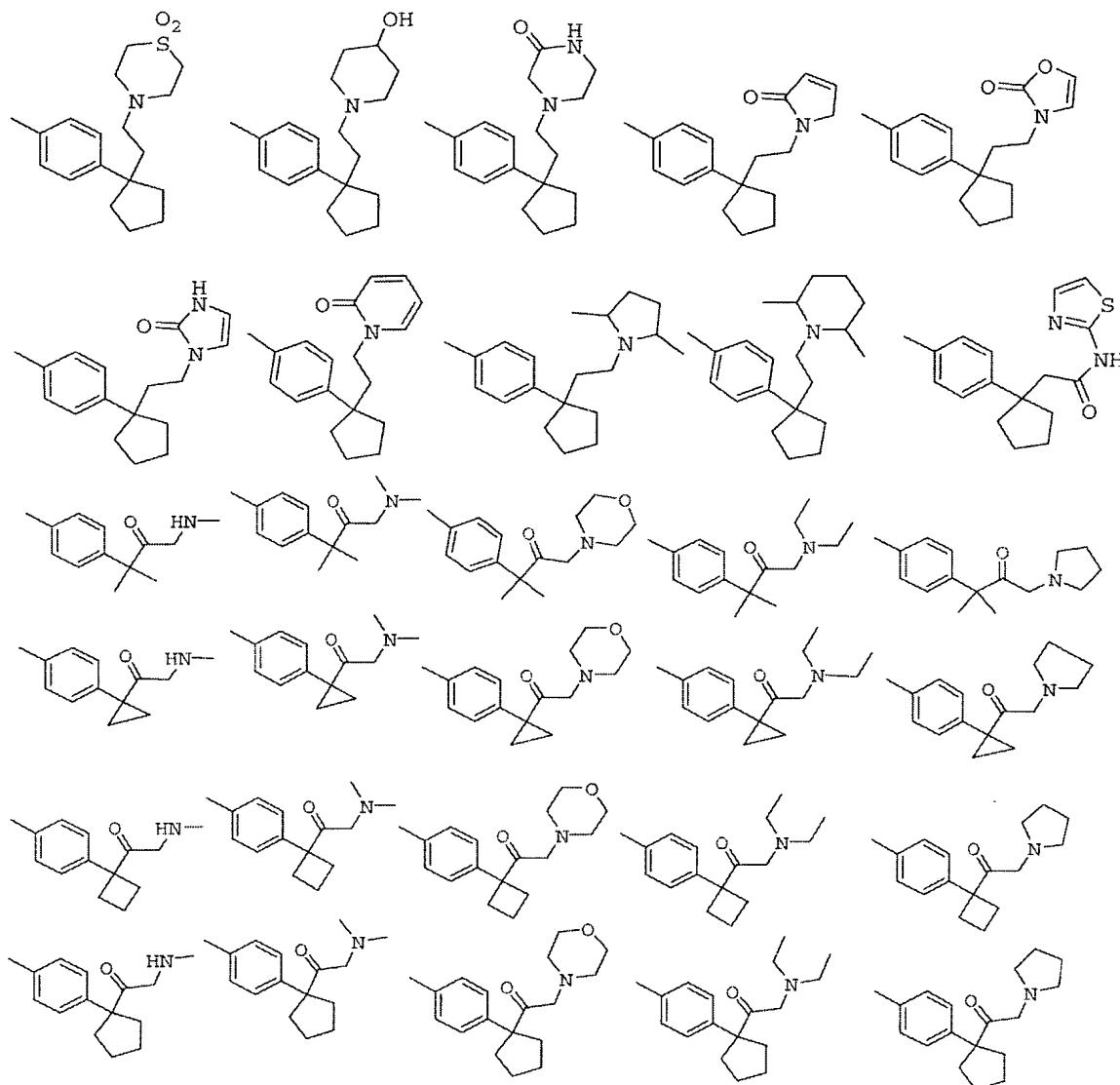












5 [8] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is selected from the group:

10 1-(4-methoxyphenyl)-6-(4-{1-[
 (methylamino)methyl]cyclopropyl}phenyl)-3-
 (trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-
 c]pyridin-7-one;

6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

5 6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

10 6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

15 6-(4-{1-[(cyclopentylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

20 1-(4-methoxyphenyl)-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

25 6-[4-(1-[(3*R*)-3-hydroxy-1-pyrrolidinylmethyl]cyclopropyl)phenyl]-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

30 6-(4-{1-[(4-hydroxy-1-piperidinyl)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

35 1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-(4-methoxyphenyl)-6-{4-[1-(1-pyrrolidinylcarbonyl)cyclopropyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

5

1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}-N,N-dimethylcyclopropanecarboxamide;

10 1-(4-methoxyphenyl)-6-(4-{1-[(4-methyl-1-piperazinyl)carbonyl]cyclopropyl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

15 6-{4-[1-(4-hydroxypiperidine-1-carbonyl)cyclopropyl]phenyl}-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

20 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropanecarboxamide;

25 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropanecarboxylic acid cyclopentylamide;

30 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}-N-(1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide;

35 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-

yl]phenyl}-N-(1*H*-tetraazol-5-yl)cyclopropanecarboxamide;

5 methyl 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclopropanecarboxylate;

10 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclopropanecarbonitrile;

15 6-{4-[1-(aminomethyl)cyclopropyl]phenyl}-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

20 N-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclopropyl]methyl]-*N*-methylacetamide;

25 N'-ethyl-*N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclopropyl]methyl]-*N*-methylurea;

30 N-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclopropyl]methyl]-*N*-methylmethanesulfonamide;

35 1-(4-methoxyphenyl)-6-{4-[1-(2-methylimidazol-1-ylmethyl)cyclopropyl]phenyl}-3-trifluoromethyl-1,4,5,6-tetrahydro-pyrazolo[3,4-*c*]pyridin-7-one;

1-(4-methoxyphenyl)-6-{4-[1-(thiazol-2-ylaminomethyl)-cyclopropyl]phenyl}-3-trifluoromethyl-1,4,5,6-tetrahydro-pyrazolo[3,4-*c*]pyridin-7-one;

methyl 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopentanecarboxylate;

5

1-(4-methoxyphenyl)-6-(4-{1-[
 (methylamino)methyl]cyclopentyl}phenyl)-3-
 (trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-
 c]pyridin-7-one;

10

6-(4-{1-[(dimethylamino)methyl]cyclopentyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

15

1-(4-methoxyphenyl)-6-{4-[1-(1-pyrrolidinylmethyl)cyclopentyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-c]pyridin-7-one;

20

6-[4-[(3*R*)-3-hydroxy-1-pyrrolidinylmethyl]cyclopentyl]phenyl]-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

25

1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopentyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-c]pyridin-7-one;

30

N-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclopentyl]methyl]-*N*-methylacetamide;

**N- [(1- { 4- [1- (4-methoxyphenyl) -7-oxo-3- (trifluoromethyl) -
1, 4, 5, 7-tetrahydro-6H-pyrazolo[3, 4-c]pyridin-6-**

yl]phenyl)cyclopentyl)methyl]-N-methylmethanesulfonamide;

5 methyl 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-
1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-
yl]phenyl}cyclobutanecarboxylate;

1 - (4-methoxyphenyl)-6- (4- {1-
[(methylamino)methyl]cyclobutyl}phenyl)-3-
10 (trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-
c]pyridin-7-one;

6-(4-{1-[(dimethylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-
15 7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-(4-{1-[(diethylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

25
6-[4-[1-[(3*R*)-3-hydroxy-1-
pyrrolidinyl]methyl]cyclobutyl]phenyl]-1-(4-
methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-
7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

30 1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclobutyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

5 *N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclobutyl)methyl]-*N*-methylacetamide;

10 *N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclobutyl)methyl]-*N*-methylmethanesulfonamide;

15 1-{4-[1-(4-Methoxyphenyl)-7-oxo-3-trifluoromethyl-1,4,5,7-tetrahydro-pyrazolo[3,4-*c*]pyridin-6-yl]-phenyl}cyclohexanecarboxylic acid methyl ester;

20 1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclohexyl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

25 6-(4-{1-[(dimethylamino)methyl]cyclohexyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

30 *N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclohexyl)methyl]-*N*-methylacetamide;

35 *N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl)cyclohexyl)methyl]-*N*-methylmethanesulfonamide;

40 1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro 7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

5 6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

10 6-(4-{1-[(cyclopentylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

15 1-(4-methoxyphenyl)-3-(methylsulfonyl)-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

20 6-[4-(1-{{(3*R*)-3-hydroxy-1-pyrrolidinylmethyl}cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

25 6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

30 1-(4-methoxyphenyl)-3-(methylsulfonyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

35 N-[(1-{4-[1-(4-methoxyphenyl)-3-(methylsulfonyl)-7-oxo-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl}phenyl)cyclopropylmethyl]-*N*-methylacetamide;

3-methanesulfonyl-1-(4-methoxyphenyl)-6-{4-[1-(2-methylimidazol-1-ylmethyl)cyclopropyl]phenyl}-1,4,5,6-tetrahydro-pyrazolo[3,4-*c*]pyridin-7-one;

3-methanesulfonyl-1-(4-methoxyphenyl)-6-{4-[1-(thiazol-2-ylaminomethyl)cyclopropyl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

5

1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclobutyl}phenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

10

6-(4-{1-[(dimethylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

15

6-(4-{1-[(isopropylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

20

1-(4-methoxyphenyl)-3-(methylsulfonyl)-6-{4-[1-(1-pyrrolidinylmethyl)cyclobutyl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

25

6-[4-(1-[(3*R*)-3-hydroxy-1-pyrrolidinylmethyl]cyclobutyl)phenyl]-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

30

6-(4-{1-[(diethylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-(4-methoxyphenyl)-3-(methylsulfonyl)-6-{4-[1-(4-morpholinylmethyl)cyclobutyl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

35

N-[(1-{4-[1-(4-methoxyphenyl)-3-(methylsulfonyl)-7-oxo-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropyl)methyl]-N-methylacetamide;

5 *1-(4-methoxyphenyl)-6-(4-{1-[methylamino]methyl}cyclopropyl)phenyl]-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;*

10 *6-(4-{1-[(dimethylamino)methyl}cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;*

15 *6-(4-{1-[(diethylamino)methyl}cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;*

20 *1-(4-methoxyphenyl)-7-oxo-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;*

25 *1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;*

30 *6-(4-{1-[(isopropylamino)methyl}cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;*

35 *6-[4-(1-{[(3R)-3-hydroxy-1-pyrrolidinyl]methyl}cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;*

35 *1-(4-methoxyphenyl)-6-(4-{1-[methylamino]methyl}cyclopropyl)phenyl]-7-oxo-*

4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carbonitrile;

6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carbonitrile;

6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carbonitrile;

1-(4-methoxyphenyl)-7-oxo-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carbonitrile;

6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carbonitrile;

6-[4-(1-[(3*R*)-3-hydroxy-1-pyrrolidinylmethyl]cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carbonitrile;

1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carbonitrile;

1-(3-chlorophenyl)-6-{4-[1-(isopropylamino)methyl]cyclopropyl}phenyl)-7-oxo-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4, 5, 6, 7-tetrahydro-1*H*-pyrazolo[3, 4-*c*]pyridine-3-carboxamide;

6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

5

1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

10 1-(3-chlorophenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

15 1-(3-chlorophenyl)-6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

20 1-(3-chlorophenyl)-6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

25 1-(3-chlorophenyl)-6-(4-{1-[(diisopropylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

30 1-(3-chlorophenyl)-6-(4-{1-[(cyclopropylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

35 1-(3-chlorophenyl)-6-(4-{1-[(cyclobutylamino)methyl]cyclopropyl}phenyl)-7-oxo-

4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-7-oxo-6-(4-{1-[(2-oxo-1-pyrrolidinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-[4-(1-[(2-hydroxyethyl)(methyl)amino]methyl)cyclopropyl]phenyl]-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-(4-{1-[2-(dimethylamino)-2-oxoethyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-{4-[1-(methoxymethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-{4-[1-(methoxymethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(3-chlorophenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(3-chlorophenyl)-6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(3-chlorophenyl)-6-[4-(1-[(2-hydroxyethyl)(methyl)amino]methyl)cyclopropyl]phenyl]-

7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[2-oxo-1-pyrrolidinyl]methyl}cyclopropyl)phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

N-[(1-{4-[3-cyano-1-(4-methoxyphenyl)-7-oxo-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclopropyl)methyl]-*N*-methylacetamide;

6-(4-{1-[(cyclopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

15 6-(4-{1-[(cyclobutylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

20 6-[4-(1-[(2-hydroxyethyl)amino)methyl]cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

25 6-[4-(1-[(2-hydroxyethyl)(methyl)amino)methyl]cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

30 6-(4-{1-[(diisopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

35 5-(4-{1-[(diisopropylamino)methyl]cyclopropyl}phenyl)-3-(4-methoxyphenyl)-3,5,6,7-tetrahydro-4*H*-[1,2,3]triazolo[4,5-*c*]pyridin-4-one;

5-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-3-(4-methoxyphenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

5 3-(4-methoxyphenyl)-5-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

3-(4-methoxyphenyl)-5-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

3-(4-methoxyphenyl)-5-(4-{1-[(2-oxo-1-pyrrolidinyl)methyl]cyclopropyl}phenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

5-[4-(1-{{(2-hydroxyethyl)amino)methyl}cyclopropyl}phenyl]-3-(4-methoxyphenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

20 3-(3-chlorophenyl)-5-[4-(1-{{(2-hydroxyethyl)amino)methyl}cyclopropyl}phenyl]-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

25 3-(3-chlorophenyl)-5-[4-(1-{{(2-hydroxyethyl)(methyl)amino)methyl}cyclopropyl}phenyl]-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

30 3-(3-chlorophenyl)-5-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

35 3-(3-chlorophenyl)-5-(4-{1-[(3-hydroxy-1-pyrrolidinyl)methyl]cyclopropyl}phenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;

6-[4-(1-[(2-hydroxyethyl)(methyl)amino]methyl)cyclopropyl]phenyl]-
1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-
5 pyrazolo[3,4-c]pyridine-3-carboxamide;

6-[4-(1-(dimethylamino)cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-
pyrazolo[3,4-c]pyridine-3-carboxamide;

10 6-(4-(1-[(2-hydroxyethyl)(methyl)amino]cyclopropyl)phenyl)-
1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-
pyrazolo[3,4-c]pyridine-3-carboxamide;

15 2-(1-{4-[1-(4-methoxyphenyl)-3-(methylsulfonyl)-7-oxo-
1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-
yl]phenyl}cyclopropyl)-N,N-dimethylacetamide;

20 6-(4-(1-[2-(dimethylamino)-2-oxoethyl)cyclopropyl)phenyl)-
1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-
pyrazolo[3,4-c]pyridine-3-carboxamide;

25 2-(1-{4-[3-cyano-1-(4-methoxyphenyl)-7-oxo-1,4,5,7-
tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-
yl]phenyl}cyclopropyl)-N,N-dimethylacetamide;

30 2-(1-{4-[3-cyano-1-(4-methoxyphenyl)-7-oxo-1,4,5,7-
tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-
yl]phenyl}cyclopropyl)acetamide;

2-(1-{4-[1-(3-chlorophenyl)-3-cyano-7-oxo-1,4,5,7-
tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-
yl]phenyl}cyclopropyl)acetamide;

1-(3-chlorophenyl)-6-(4-{1-[2-(dimethylamino)-2-oxoethyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

5 2-(1-{4-[1-(3-chlorophenyl)-3-(methylsulfonyl)-7-oxo-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclopropyl)-*N,N*-dimethylacetamide;

10 2-(1-{4-[3-(3-chlorophenyl)-4-oxo-3,4,6,7-tetrahydro-5*H*-[1,2,3]triazolo[4,5-*c*]pyridin-5-yl]phenyl}cyclopropyl)-*N,N*-dimethylacetamide;

15 2-(1-{4-[3-(4-methoxyphenyl)-4-oxo-3,4,6,7-tetrahydro-5*H*-[1,2,3]triazolo[4,5-*c*]pyridin-5-yl]phenyl}cyclopropyl)-*N,N*-dimethylacetamide;

20 2-(1-{4-[3-(4-methoxyphenyl)-4-oxo-3,4,6,7-tetrahydro-5*H*-[1,2,3]triazolo[4,5-*c*]pyridin-5-yl]phenyl}cyclopropyl)acetamide;

25 1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(2-oxo-1-imidazolidinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

30 1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(2-oxo-1-piperazinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

35 1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(3-oxo-4-morpholinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(2-oxo-1-piperidinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;